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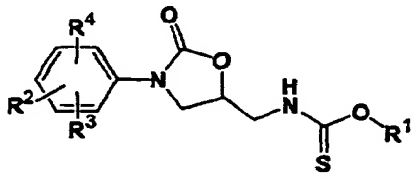
(54) THIOCARBAMIC ACID DERIVATIVES

(57) Thiocarbamic acid derivatives represented by the following general formula or salts thereof which are useful as antibacterial agents:



wherein R^1 represents an alkyl group which may be substituted, or a cycloalkyl group which may be substituted; and R^2, R^3, and R^4 independently represent hydrogen atom, a halogen atom, an alkyl group which may be substituted, an alkogyl group which may be substituted, an amino group which may be substituted, an alkanoyl group which may be substituted, a cycloalkyloxy group which has a heteroatom as a ring constituting atom and which may be substituted, or a saturated heterocyclic group which may be substituted; or any two of R^2, R^3, and R^4 may bind to each other to form, together with the benzene ring, a condensed hydrocarbon ring which may be substituted.

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Description

Technical Field

[0001] The present invention relates to novel thiocarbamic acid derivatives or salts thereof which are useful as medicaments, particularly as antibacterial agents.

Background Art

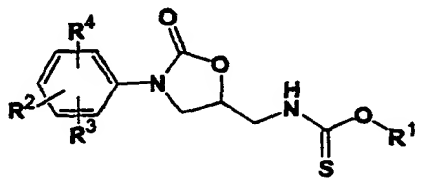
[0002] As compounds having the 3-aryl-2-oxooxazolidine structure which are analogous to the compounds according to the present invention, Japanese Patent Unexamined Publication No.(Sho) 60-8277, Journal of Medicinal Chemistry, Vol. 39, p.673 (1996) and the like disclose N-[(3-aryl-2-oxooxazolidin-5-yl)methyl]acetamide derivatives; Current Pharmaceutical Design, Vol. 2, p.175 (1996), Journal of Medicinal Chemistry, Vol. 32, p.1673 (1989) and the like disclose 3-aryl-5-hydroxymethyl-2-oxooxazolidine derivatives, 3-aryl-5-halogenomethyl-2-oxooxzolidine derivatives and the like; and Japanese Patent Unexamined Publication No.(Hei) 9-316073 and the like disclose N-(3-heteroaryl-2-oxooxazolidin-5-yl)methylthioacetamide derivatives, N-(3-heteroaryl-2-oxooxazolidin-5-yl)methyl-N'-methylthiourea derivatives and the like. These compounds are described to have antibacterial activities against Gram-positive bacteria. However, the antibacterial activities of these compounds are insufficient, and development of more excellent antibacterial agents has been desired.

[0003] Various antibacterial agents such as antibiotics and synthetic antibacterial agents, each having different mechanism of action, have been clinically used as therapeutic agents for infectious diseases. Upon the use of these antibacterial agents, appearance of multiple drug-resistant bacteria including bacteria such as Methicillin-resistant Staphylococcus aureus (MRSA) has become a worldwide problem. In patients having an underlying disease and being subjected to chemotherapy, those being subjected to administration of an immunosuppressive agent in organ transplantation, and those suffering from AIDS or another disease as so-called immunocompromized hosts, increase in opportunistic infection has been recognized, and development of chemotherapy for diseases caused by atypical acid-fast microorganism has especially desired for which only a few effective antibacterial - agents are available. Moreover, need of chemotherapy of infectious diseases caused by Mycobacterium avium complex (Mycobacterium avium, Mycobacterium intracellulare) among atypical acid-fast microorganisms have become a serious problem. The object of the present invention is to provide compounds which have excellent antibacterial activity against clinically isolated strains and atypical acid-fast microorganisms including multiple drug-resistant bacteria as well as type bacteria.

Disclosure of the Invention

[0004] The inventors of the present invention made intensive studies to achieve the aforementioned object. As a result, they found that novel thiocarbamic acid derivatives represented by the following general formula or salts thereof have excellent antibacterial activity against clinically isolated strains and atypical acid-fast microorganisms including multiple drug-resistant bacteria as well as type bacteria. The present invention was achieved on the basis of the above findings.

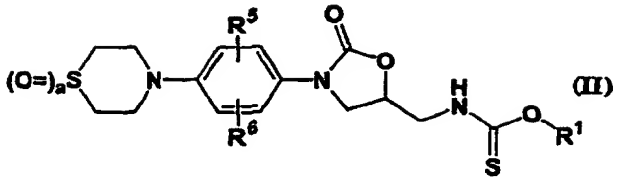
[0005] The present invention thus relates to novel thiocarbamic acid derivatives represented by the following general formula (I) or salts thereof:



(I)

wherein R^1 represents an alkyl group which may be substituted, or a cycloalkyl group which may be substituted; and R^2, R^3 and R^4 independently represent hydrogen atom, a halogen atom, an alkyl group which may be substituted, an alkoxyl group which may be substituted, an amino group which may be substituted, an alkanoyl group which may be substituted, a cycloalkyloxy group which has a heteroatom as a ring constituting atom and which may be substituted, or a saturated heterocyclic group which may be substituted; or any two of R^2, R^3 and R^4 may bind to each other to form, together with the benzene ring, a condensed hydrocarbon ring which may be substituted.

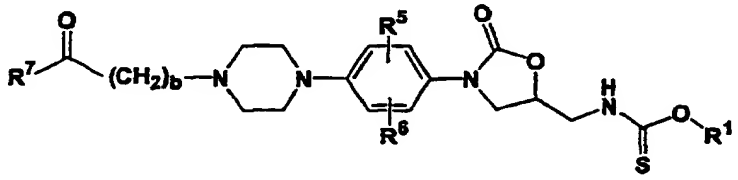
[0006] According to the second embodiment of the present invention, there are provided novel thiocarbamic acid derivatives represented by the following general formula (II) or salts thereof:



(II)

wherein R^5 and R^6 independently represent hydrogen atom, or a halogen atom; and symbol "a" represents an integer of from 0 to 2; and R^1 has the same meaning as that defined above.

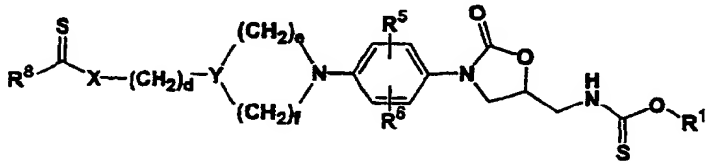
[0007] According to the third embodiment of the present invention, there are provided novel thiocarbamic acid derivatives represented by the following general formula (III) or salts thereof:



(III)

wherein R^7 represents an alkyl group which may be substituted, an amino group which may be substituted, or an alkoxyl group which may be substituted; and symbol "b" represents an integer of from 1 to 4; and R^1, R^5 and R^6 have the same meanings as those defined above.

[0008] According to the forth embodiment of the present invention, there are provided novel thiocarbamic acid derivatives represented by the following general formula (IV) or salts thereof:



(IV)

wherein R^8 represents an alkyl group which may be substituted, a cycloalkyl group which may be substituted, an alkenyl group which may be substituted, an alkynyl group which may be substituted, an alkoxyl group which may be substituted, an alkylthio group which may be substituted, an amino group which may be substituted, a saturated heterocyclic group which may be substituted, an aryl group which may be substituted, or an aralkyl group which may be substituted; Y represents CH or nitrogen atom; X represents NH or single bond; symbol "d" represents an integer of from 0 to 3; symbols "e" and "f" independently represent an integer of from 1 to 3; and R^1, R^5 and R^6 have the same meanings as those defined above.

[0009] According to another aspect of the present invention, there is provided a medicament which comprises as an active ingredient the aforementioned thiocarbamic acid derivative or the salt thereof. The medicament provided by the present invention can be suitably used, for example, as an antibacterial agent.

[0010] According to a further aspect, there are provided a use of the aforementioned thiocarbamic acid derivative or the salt thereof for the manufacture of the aforementioned medicament; and a method for preventive and/or therapeutic treatment of infectious diseases, which comprises the step of administering a preventively and/or therapeutically effective amount of the aforementioned thiocarbamic acid derivative or the salt thereof to a mammal including a human.

Best Mode for Carrying Out the Invention

[0011] Specific explanations of the novel thiocarbamic acid derivatives represented by the aforementioned general formulas (I) to (IV) of the present invention will be given below. The compounds represented by the aforementioned general formulas (II) to (IV) are characterized in that any two of R^2, R^3 and R^4 are independently hydrogen atom or a halogen atom in the aforementioned general formula (I). However, the scope of the present invention is not limited to the compounds represented by the aforementioned general formulas (II) to (IV), and it should be understood that any compounds which have, as any two of R^2, R^3 and R^4, substituents other than hydrogen atom or a halogen atom among

those defined in the aforementioned general formula (I) fall within the scope of the present invention.

[0012] In the aforementioned general formulas (I) to (IV) according to the present invention, the alkyl group represented by R^1, R^2, R^3, R^4, R^7 or R^8 includes a straight or branched chain alkyl group, or cyclic alkyl group or an alkyl group as a combination thereof having from 1 to 6 carbon atoms, preferably a straight or branched chain alkyl group. Examples include methyl group, ethyl group, n-propyl group, isopropyl group, n-butyl group, isobutyl group, sec-butyl group, tert-butyl group, n-pentyl group, isopentyl group, neopentyl group, n-hexyl group and the like. The cycloalkyl group represented by R^1 or R^8 includes a cycloalkyl group having from 3 to 6 carbon atoms. Examples include cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group and the like. The halogen atom represented by R^2, R^3, R^4, R^5 or R^6 includes fluorine atom, chlorine atom, bromine atom, and iodine atom. The alkoxyl group represented by R^2, R^3, R^4, R^7 or R^8 includes a straight or branched chain alkyl group having from 1 to 6 carbon atoms. Examples include methoxy group, ethoxy group, n-propoxy group, isopropoxy group, n-butoxy group, isobutoxy group, sec-butoxy group, tert-butoxy group, n-pentyloxy group, isopentyloxy group, neopentyloxy group, n-hexyloxygroup and the lik .

[0013] In the aforementioned general formulas (I) and (IV) according to the present invention, the alkanoyl group represented by R^2, R^3 or R^4 includes, for example, formyl group, acetyl group, propionyl group, butyryl group, isobutyryl group, valeryl group, isovaleryl group, hexanoyl group, heptanoyl group and the like. The cycloalkyloxy group represented by R^2, R^3 or R^4 which has a heteroatom as a ring constituting atom includes, for example, aziridinyloxy group, azetidinyloxy group, pyrrolidinyloxy group, piperidyloxy group, hexahydro-1H-azepin-1-yloxy group, oxetanyloxy group, tetrahydrofuranyloxy group, tetrahydropyranyloxy group, thietanyloxy group, tetrahydrothiophenyloxy group, tetrahydrothiopyranyloxy group, oxazolidinyloxy group, thiazolidinyloxy group, piperazinyloxy group, morpholinyloxy group, thiomorpholinyloxy group, 1-oxidothiomorpholinyloxy group, 1,1-dioxidothiomorpholinyloxy group, hexahydro-1H-1,4-diazepin-1-yloxy group, 3-azabicyclo[3.3.0]octanyloxy group, 3,7-diazabicyclo[3.3.0]octanyloxy group and the like. The saturated heterocyclic group represented by R^2, R^3, R^4 or R^8 includes, for example, aziridinyl group, azetidinyl group, pyrrolidinyl group, oxazolidinyl group, thiazolidinyl group, piperidyl group, piperazinyl group, oxetanyl group, tetrahydrofuranyl group, tetrahydropyranyl group, thietanyl group, tetrahydrothiophenyl group, tetrahydrothiopyranyl group, thiomorpholinyl group, 1-oxidethiomorpholinyl group, 1,1-dioxidothiomorpholinyl group, hexahydro-1H-azepin-1-yl group, hexahydro-1H-1,4-diazepin-1-yl group, 3-azabicyclo[3.3.0]octanyl group, 3,7-diazabicyclo[3.3.0]octanyl group and the like.

[0014] In the aforementioned general formula (I) according to the present invention, when any two of R^2, R^3 and R^4 bind to each other to form a condensed hydrocarbon ring together with the benzene ring, the condensed ring group includes, for example, indan-5-yl group, 1-indanon-5-yl group, inden-5-yl group, inden-6-yl group, 1-indanon-6-yl group, 2-indanon-5-yl group, 1,3-indandion-5-yl group, naphthalen-2-yl group, 1(2H)-naphthalenon-6-yl group, 1(2H)-naphthalenon-7-yl group, 1,2,3,4-tetrahydronaphthalen-6-yl group, 1,2,3,4-tetrahydro-1-naphthalenon-6-yl group, 1,2,3,4-tetrahydro-1-naphthalenon-7-yl group, 1,2,3,4-tetrahydro-2-naphthalenon-6-yl group, 1,2,3,4-tetrahydro-2-naphthalenon-7-yl group, 1,2-naphthoquinon-6-yl group, 1,2-naphthoquinon-7-yl group, 1,4-naphthoquinon-6-yl group, fluoren-2-yl group, fluoren-3-yl group, fluorenon-2-yl group, fluorenon-3-yl group, anthracen-1-yl group, anthracen-2-yl group and the like.

[0015] In the aforementioned general formula (IV) according to the present invention, the alkenyl group represented by R^8 includes a straight or branched chain alkenyl group having from 2 to 4 carbon atoms, for example, vinyl group, propenyl group, 2-methylpropenyl group, butenyl group, butadienyl group and the like. The alkynyl group includes an alkynyl group having from 2 to 4 carbon atoms, for example, ethynyl group, propynyl group, butynyl group and the like. The alkylthio group represented by R^8 includes an alkylthio group which comprises a straight or branched chain alkyl group having from 1 to 6 carbon atoms, for example, methylthio group, ethylthio group, n-propylthio group, isopropylthio group, n-butylthio group, isobutylthio group, sec-butylthio group, tert-butylthio group, n-pentylthio group, isopentylthio group, neopentylthio group, n-hexylthio group and the like. The aryl group represented by R^8 means an aromatic ring group which encompasses ring systems containing two or more rings optionally having a heteroatom as a ring constituting atom. Examples include phenyl group, pyridin-2-yl group, pyridin-3-yl group, pyridin-4-yl group, pyrazin-2-yl group, pyrimidin-2-yl group, pyrimidin-4-yl group, pyrimidin-5-yl group, furan-2-yl group, furan-3-yl group, thiophen-2-yl group, thiophen-3-yl group, pyrrol-1-yl group, pyrrol-2-yl group, pyrrol-3-yl group, pyrazol-1-yl group, pyrazol-3-yl group, pyrazol-4-yl group, imidazol-1-yl group, imidazol-2-yl group, imidazol-4-yl group, 1H-1,2,3-triazol-1-yl group, 1H-1,2,3-triazol-4-yl group, 1H-1,2,4-triazol-1-yl group, 1H-1,2,4-triazol-3-yl group, 1H-1,2,4-triazol-5-yl group, tetrazol-1-yl group, tetrazol-5-yl group, oxazol-2-yl group, oxazol-4-yl group, oxazol-5-yl group, thiazol-2-yl group, thiazol-4-yl group, thiazol-5-yl group, naphthalen-1-yl group, naphthalen-2-yl group, benzofuran-2-yl group, benzofuran-3-yl group, benzofuran-4-yl group, benzofuran-5-yl group, benzofuran-6-yl group, benzofuran-7-yl group, benzo[b]thiophen-2-yl group, benzo[b]thiophen-3-yl group, benzo[b]thiophen-4-yl group, benzo[b]thiophen-5-yl group, benzo[b]thiophen-6-yl group, benzo[b]thiophen-7-yl group, indol-1-yl group, indol-2-yl group, indol-3-yl group, indol-4-yl group, indol-5-yl group, indol-6-yl group, indol-7-yl group, benzimidazol-1-yl group, benzimidazol-2-yl group, benzimidazol-4-yl group, benzimidazol-5-yl group, benzotriazol-1-yl group, benzotriazol-4-yl group, benzotriazol-5-yl group, benzoxazol-2-yl

group, benzoxazol-4-yl group, benzoxazol-5-yl group, benzoxazol-6-yl group, benzoxazol-7-yl group, benzothiazol-2-yl group, benzothiazol-4-yl group, benzothiazol-5-yl group, benzothiazol-6-yl group, benzothiazol-7-yl group and th like. The aralkyl group represented by R^8 means an alkyl group having from 1 to 4 carbon atoms which is substituted with the aforementioned aryl group at any position. Examples include benzyl group, phenethyl group, phenylpropyl group, phenylbutyl group, triphenylmethyl group, (pyridin-2-yl)methyl group, (pyrazin-2-yl)methyl group, (pyrimidin-2-yl)methyl group, (furan-2-yl)methyl group, (thiophen-2-yl)methyl group, (pyrrol-1-yl)methyl group, (pyrazol-1-yl)methyl group, (imidazol-1-yl)methyl group, (1H-1,2,3-triazol-1-yl)methyl group, (1H-1,2,4-triazol-1-yl)methyl group, (tetrazol-5-yl)methyl group, (oxazol-2-yl)methyl group, (thiazol-2-yl)methyl group, (naphthalen-1-yl)methyl group, (benzofuran-2-yl)methyl group, (benzo[b]thiophen-2-yl)methyl group, (indol-1-yl)methyl group, (benzimidazol-1-yl)methyl group, (benzotriazol-1-yl)methyl group, (benzoxazol-2-yl)methyl group, (benzothiazol-2-yl)methyl group and the like.

[0016] In the present specification, a substituting/binding position of "cycloalkyloxy group which has a heteroatom as a ring constituting atom", "saturated heterocyclic group", "condensed hydrocarbon ring formed together with the benzene ring", "aryl group" and "aralkyl group" may be at any position on a substitutable/bindable atom among ring-consituting elements, otherwise a substituting/binding position is specifically limited as some examples given above.

[0017] In the present specification, when certain functional groups are defined as "which may be substituted," the number and kind of substituents are not particularly limited. When two or more substituents exist, they may be the same or different. Such substituents include, for example, alkyl groups, cycloalkyl groups, hydroxyl group, mercapto group, alkoxyl groups, alkylthio groups, halogen atoms, amino group, alkylamino groups, dialkylamino groups, cyano group, cyanoalkyl groups, nitro group, formyl group, alkoxycarbonyl groups, alkoxyalkyl groups, alkoxycarbonylalkyl groups, carboxyalkyl groups, hydroxyalkanoyl groups, alkoxyalkoxyl groups, alkoxyalkanoyl groups, benzyloxycarbonyl group, benzyloxyalkanoyl groups, alkylaminoalkoxyl groups, dialkylaminoalkoxyl groups, alkylaminoalkyl groups, dialkylaminoalkyl groups, halogenoalkyl groups, oxo group, hydroxyimino group, alkoxyimino groups, aryloxyimino groups, carboxyl group, alkanoyl groups, alkanoylalkyl groups, carbamoyl group, aryl groups, aralkyl groups, phthalimido group, phthalimidoalkyl groups, alkylsulfonylamino groups, alkylcarbonylamino groups, alkylthiocarbonyl groups, alkenylthiocarbonyl groups, alkoxythiocarbonyl groups, alkoxythiocarbonylalkyl groups, thiocarbamoyl group, N-alkylthiocarbamoyl groups, N,N-dialkylthiocarbamoyl groups, azetidinylthiocarbonyl group, pyrrolidinylthiocarbonyl group, piperazinylthiocarbonyl group, morpholinylthiocarbonyl group, thiomorpholinylthiocarbonyl group, alkylthiothiocarbonyl groups, arylthiocarbonyl groups, aralkylthiocarbonyl groups, alkylthiocarbonylamino groups, alkylthiocarbonylaminoalkyl groups, alkoxythiocarbonylamino groups, alkoxythiocarbonylaminoalkyl groups, N-alkylthiocarbamoylamino groups, N,N-dialkylthiocarbamoylamino groups, alkylthiothiocarbonylamino groups, alkylthiothiocarbonylaminoalkyl groups, arylthiocarbonylamino groups, aralkylthiocarbonylamino groups, thiocarbamoylalkyl groups, N-alkylthiocarbamoylalkyl groups, N,N-dialkylcarbamoylalkyl groups, alkanoylaminoalkyl groups, alkoxythiocarbonylaminoalkyl groups, alkylsulfonylaminoalkyl groups, alkanoylalkylthiocarbonyl groups, alkylthiocarbonylalkylthiocarbonyl groups, thiocarbamoylaminoalkyl groups, N-alkylthiocarbamoylaminoalkyl groups, N,N-dialkylthiocarbamoylaminoalkyl groups, alkanoylalkylaminothiocarbonyl groups, alkylthiocarbonylalkylaminothiocarbonyl groups, alkylthiocarbonylalkyl groups, alkylthiothiocarbonylalkyl groups, alkoxythiocarbonylalkyl groups, thiocarbamoylamino group, cycloalkylthiocarbonyl groups, cycloalkylthiocarbonylamino groups, alkynylthiocarbonyl groups, alkynylthiocarbonylamino groups, thiocarbamoylalkylaminothiocarbonyl groups, N-alkylthiocarbamoylalkylaminothiocarbonyl groups, N,N-dialkylthiocarbamoylalkylaminothiocarbonyl groups and the like.

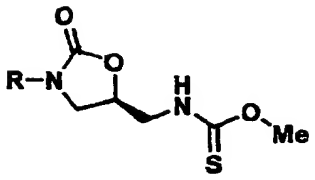
[0018] The thiocarbamic acid derivatives of the present invention have one asymmetric carbon atom in the oxazolidine ring, and may further have one or more asymmetric carbons depending on type of a substituent. The asymmetric carbons existing in the compounds of the present invention may be independently in the (R)- or (S)-configuration, and stereoisomers such as optical isomers and diastereoisomers may exist on the basis of one or more asymmetric carbons. Any stereoisomers in pure forms, any mixure of the stereoisomers, racemates and the like fall within the scope of the present invention.

[0019] The thiocarbamic acid derivatives of the present invention can be converted into salts, preferably pharmacologically acceptable salts, if desired; and the salts generated can also be converted into compounds in free forms. The salts of the compounds of the present invention are preferably the pharmacologically acceptable salts. As the acid-additive salts, there can be used, for example, salts with mineral acids such as hydrochloric acid, hydrobromic acid, nitric acid, sulfuric acid, hydroiodic acid, and phosphoric acid; and salts with organic acids such as acetic acid, propionic acid, butyric acid, formic acid, valeric acid, maleic acid, fumaric acid, citric acid, oxalic acid, malic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, trifluoroacetic acid, benzoic acid, p-toluenesulfonic acid, mandelic acid, 10-camphorsulfonic acid, tartaric acid, lactic acid, stearic acid, nicotinic acid, gluconic acid, 5-oxotetrahydrofuran-2-carboxylic acid, and 2-hydroxyglutaric acid. As the alkali-additive salts, there can be used, for example, inorganic alkali salts such as sodium salt, potassium salt, calcium salt, magnesium salt, and ammonium salt; and salts with organic bases such as ethanolamine, N,N-dialkylethanolamine, triethanolamine, piperidine, piperazine, morpholine, and thiomorpholine.

[0020] The thiocarbamic acid derivatives of the present invention or the salts thereof may exist as any crystal form

depending on manufacturing conditions, or may exist as any hydrate or solvate. These crystal forms, hydrates, and solvates, and mixtures thereof fall within the scope of the present invention.

[0021] Preferred compounds of the present invention include the following compounds; however, the present invention is not limited to these examples. The abbreviations in the tables have the following meanings: Me: methyl group; Et: ethyl group; n-Pr: n-propyl group; i-Pr: isopropyl group; n-Bu: n-butyl group; i-Bu: isobutyl group; tert-Bu: tert-butyl group; n-Pent: n-pentyl group; n-Hex: n-hexyl group; Ph: phenyl group; Bn: benzyl group; Ms: mesyl group; and, Boc: tert-butoxycarbonyl group.



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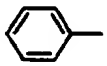
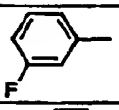
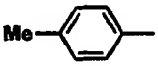
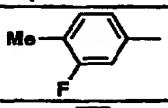
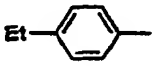
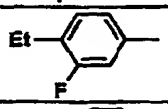
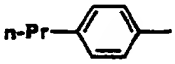
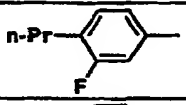
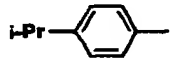
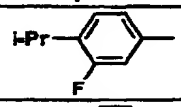
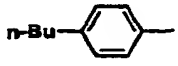
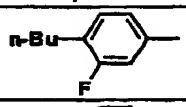
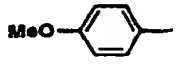
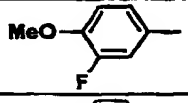
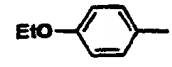
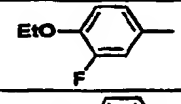
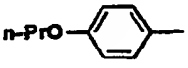
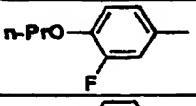
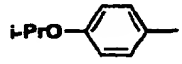
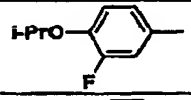
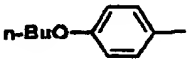
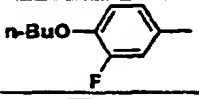
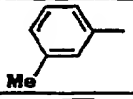
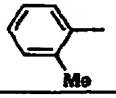
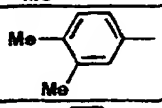
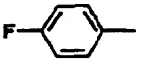
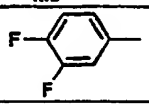
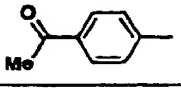
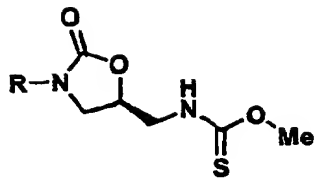
1		2	
3		4	
5		6	
7		8	
9		10	
11		12	
13		14	
15		16	
17		18	
19		20	
21		22	
23		24	
25		26	
27		28	



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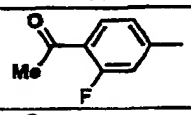
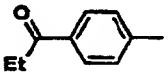
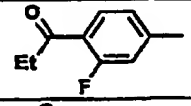
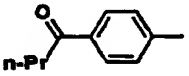
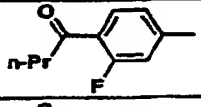
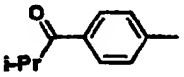
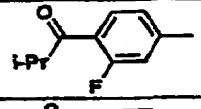
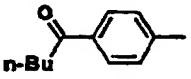
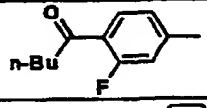
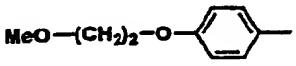
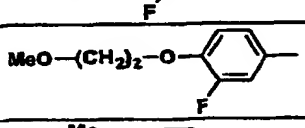
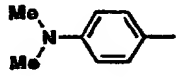
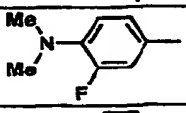
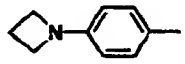
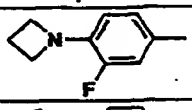
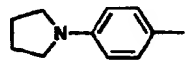
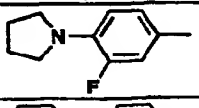
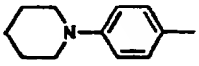
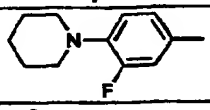
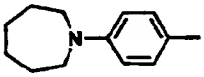
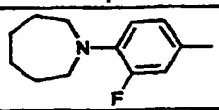
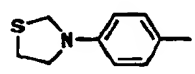
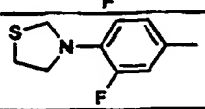
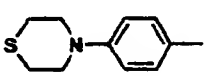
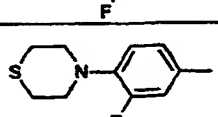
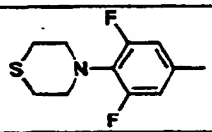
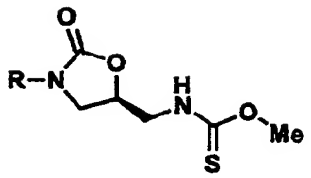
29		30	
31		32	
33		34	
35		36	
37		38	
39		40	
41		42	
43		44	
45		46	
47		48	
49		50	
51		52	
53		54	



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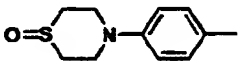
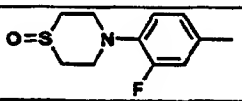
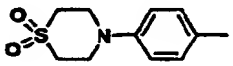
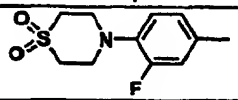
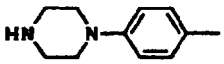
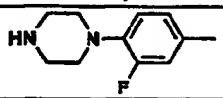
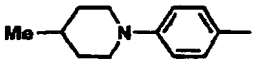
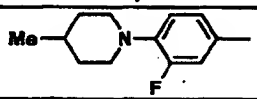
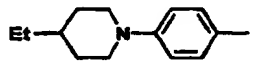
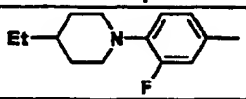
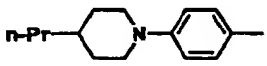
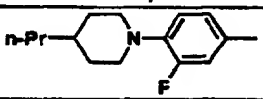
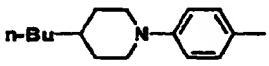
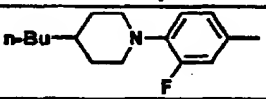
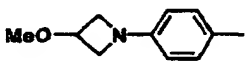
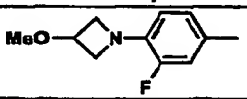
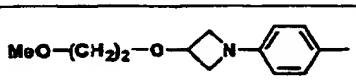
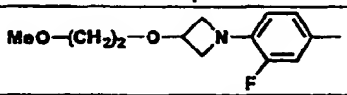
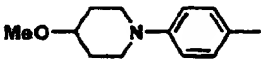
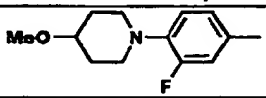
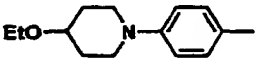
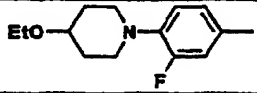
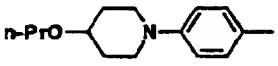
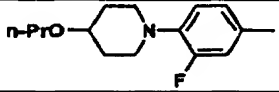
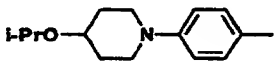
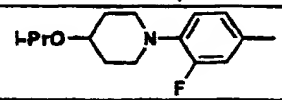
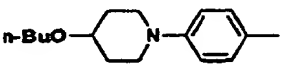
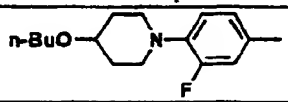
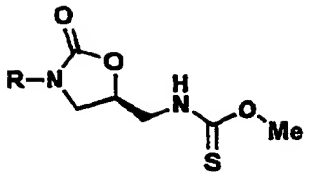
55		56	
57		58	
59		60	
61		62	
63		64	
65		66	
67		68	
69		70	
71		72	
73		74	
75		76	
77		78	
79		80	
81		82	



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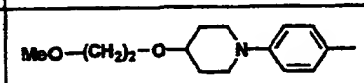
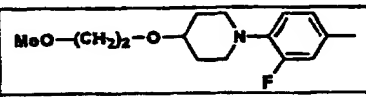
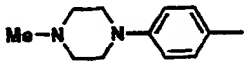
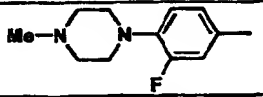
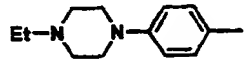
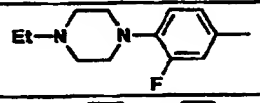
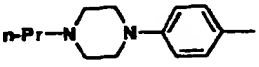
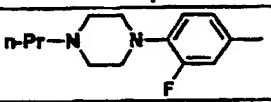
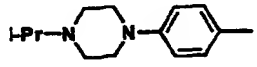
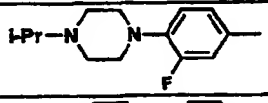
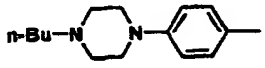
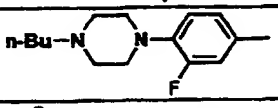
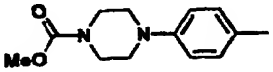
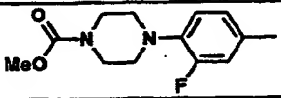
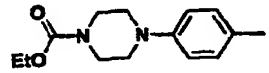
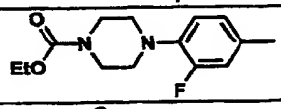
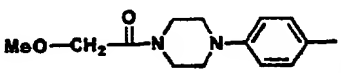
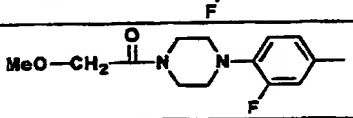
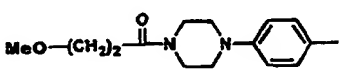
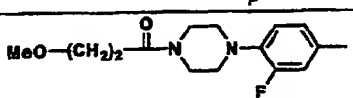
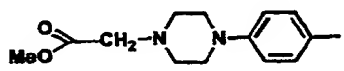
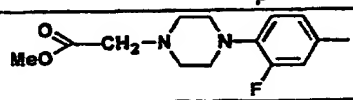
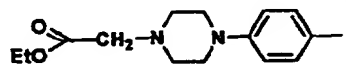
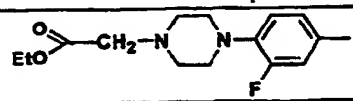
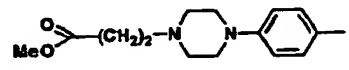
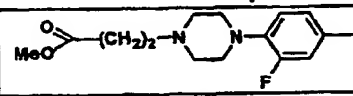
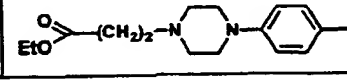
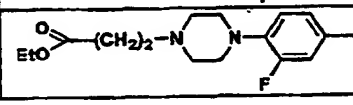
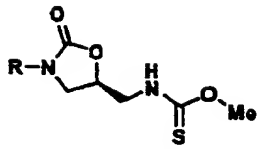
83		84	
85		86	
87		88	
89		90	
91		92	
93		94	
95		96	
97		98	
99		100	
101		102	
103		104	
105		106	
107		108	
109		110	



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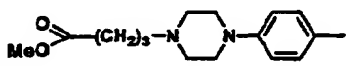
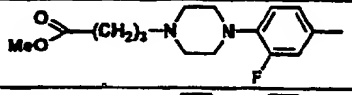
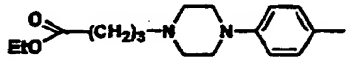
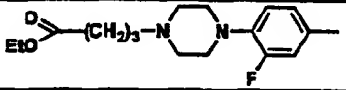
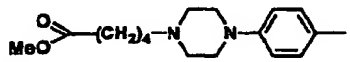
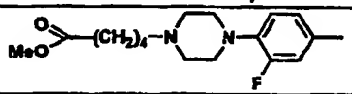
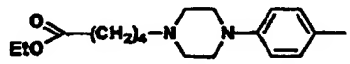
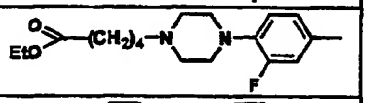
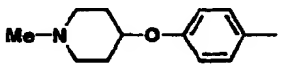
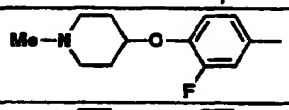
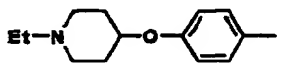
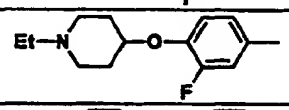
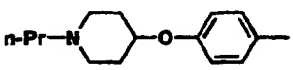
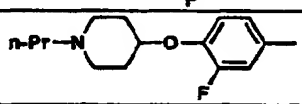
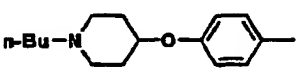
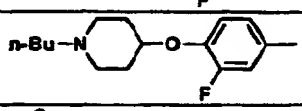
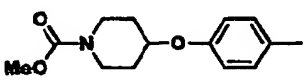
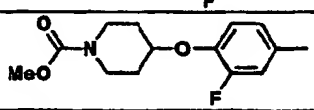
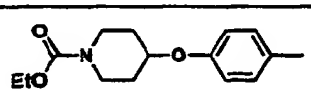
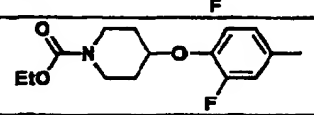
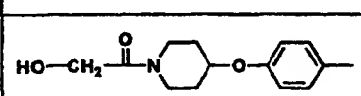
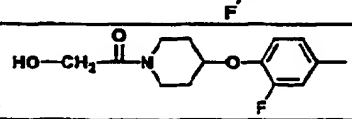
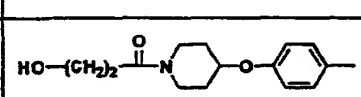
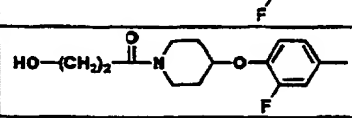
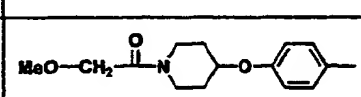
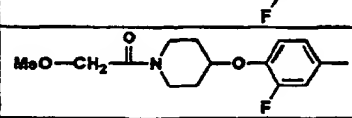
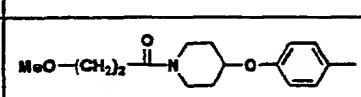
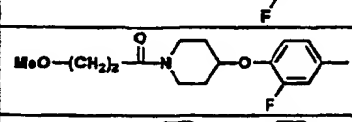
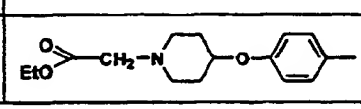
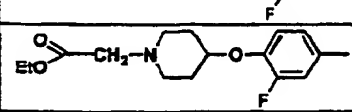
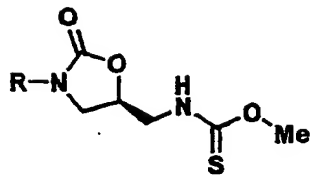
111		112	
113		114	
115		116	
117		118	
119		120	
121		122	
123		124	
125		126	
127		128	
129		130	
131		132	
133		134	
135		136	
137		138	
139		140	



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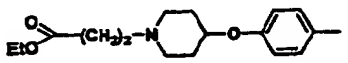
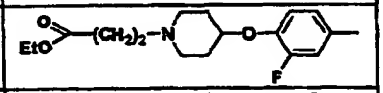
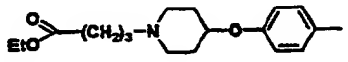
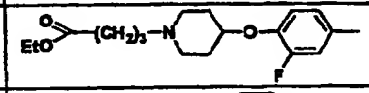
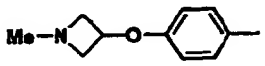
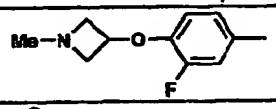
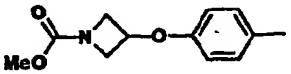
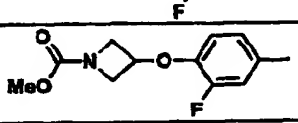
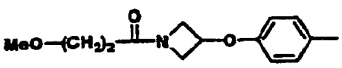
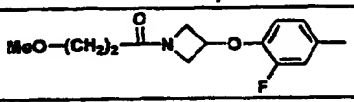
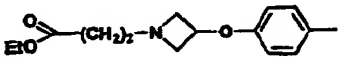
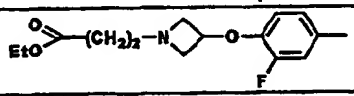
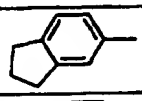
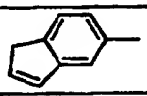
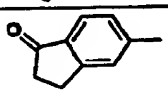
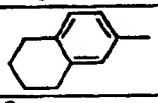
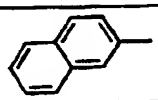
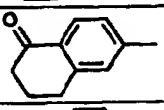
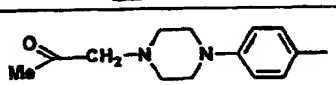
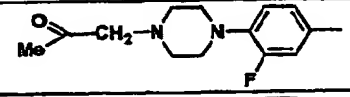
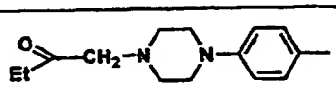
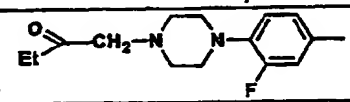
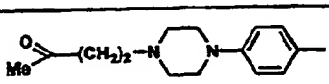
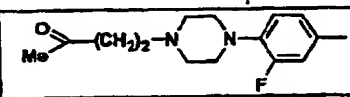
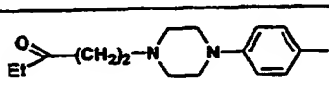
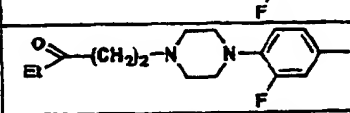
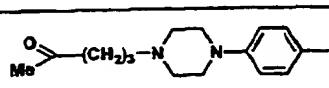
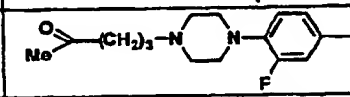
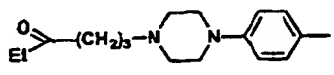
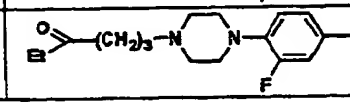
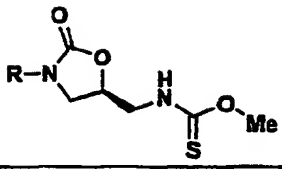
141		142	
143		144	
145		146	
147		148	
149		150	
151		152	
153		154	
155		156	
157		158	
159		160	
161		162	
163		164	
165		166	
167		168	
169		170	



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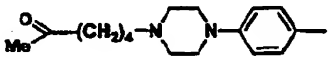
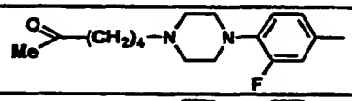
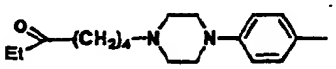
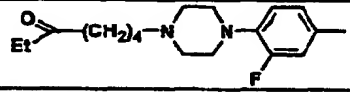
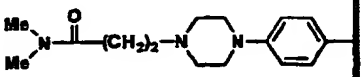
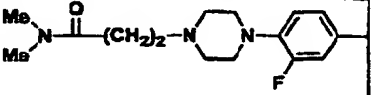
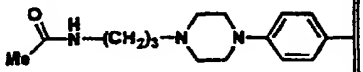
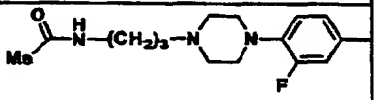
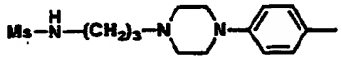
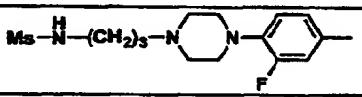
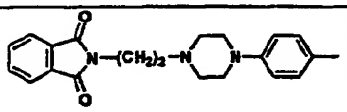
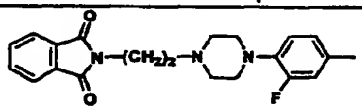
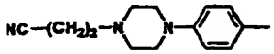
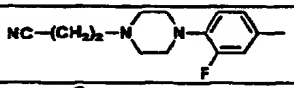
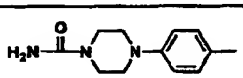
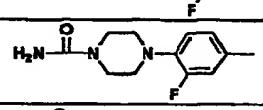
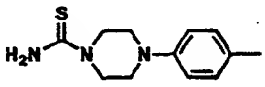
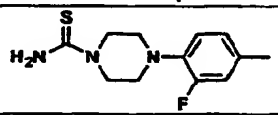
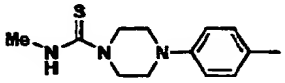
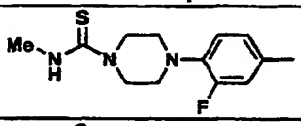
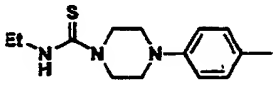
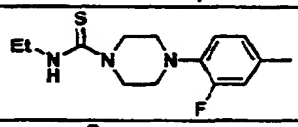
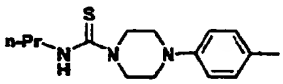
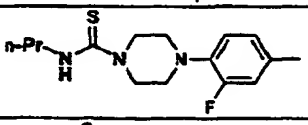
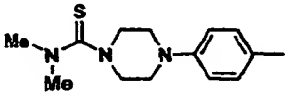
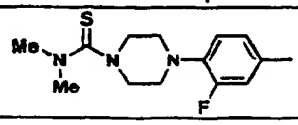
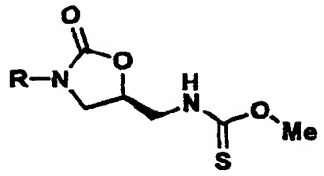
171		172	
173		174	
175		176	
177		178	
179		180	
181		182	
183		184	
185		186	
187		188	
189		190	
191		192	
193		194	
195		196	



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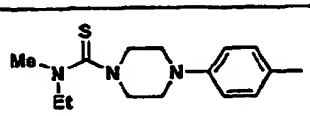
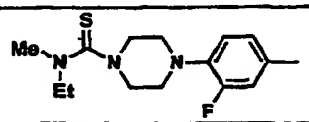
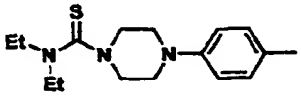
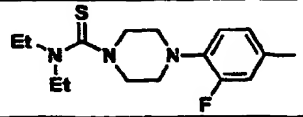
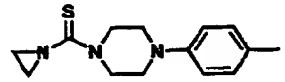
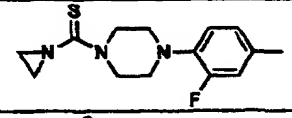
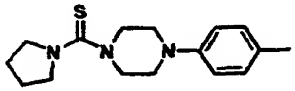
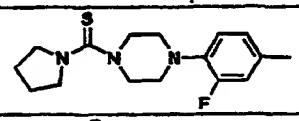
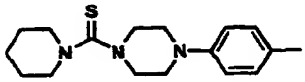
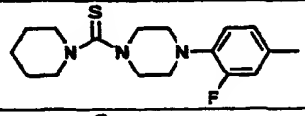
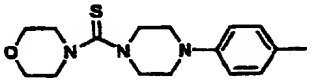
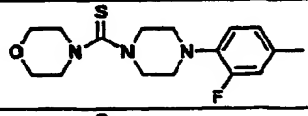
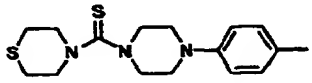
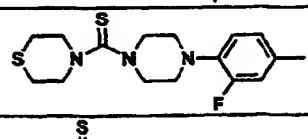
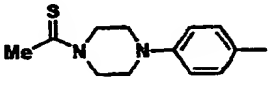
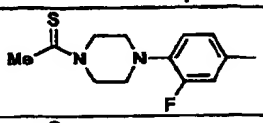
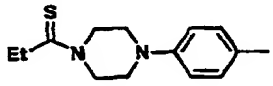
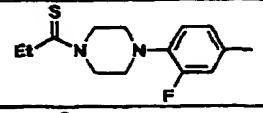
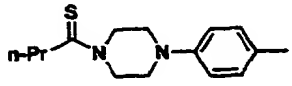
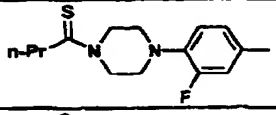
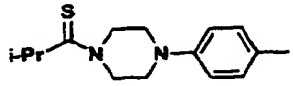
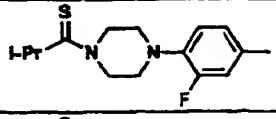
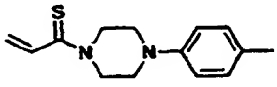
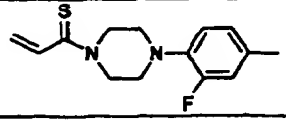
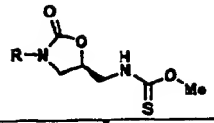
197		198	
199		200	
201		202	
203		204	
205		206	
207		208	
209		210	
211		212	
213		214	
215		216	
217		218	
219		220	



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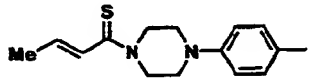
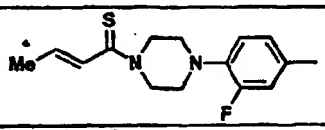
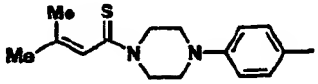
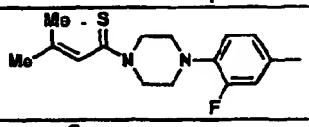
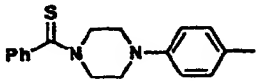
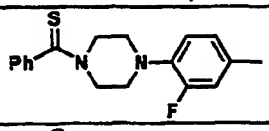
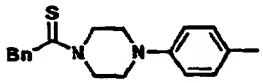
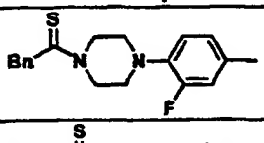
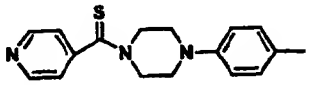
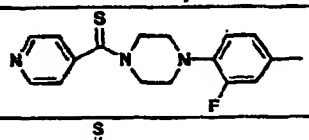
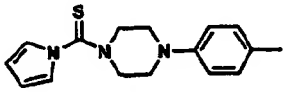
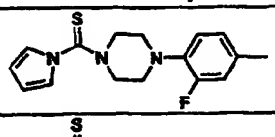
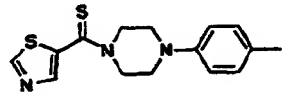
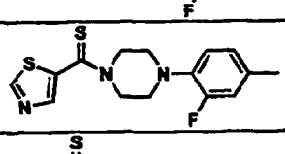
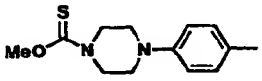
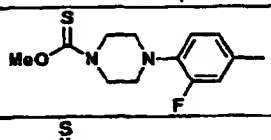
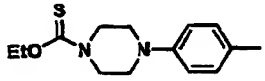
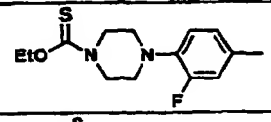
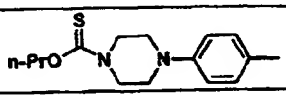
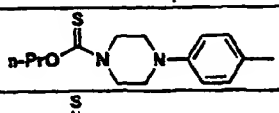
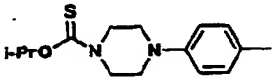
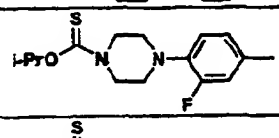
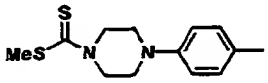
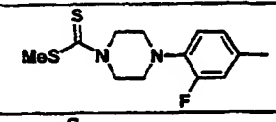
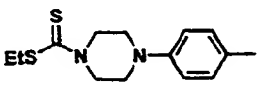
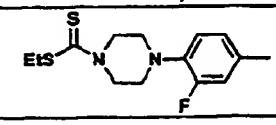
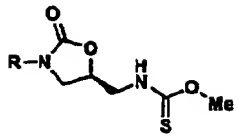
221		222	
223		224	
225		226	
227		228	
229		230	
231		232	
233		234	
235		236	
237		238	
239		240	
241		242	
243		244	
245		246	



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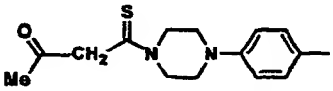
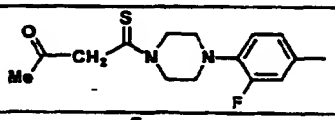
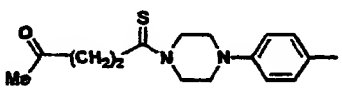
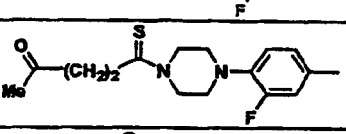
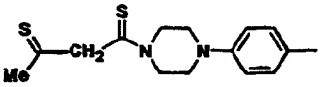
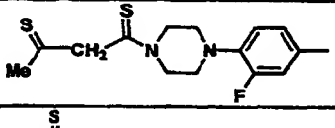
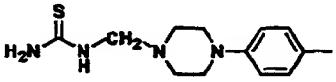
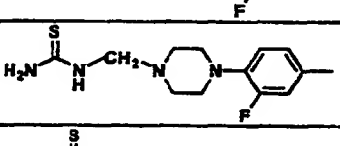
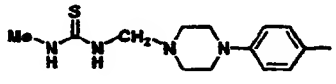
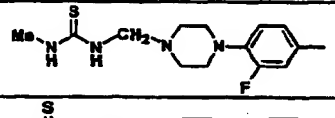
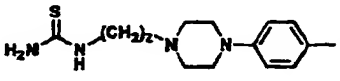
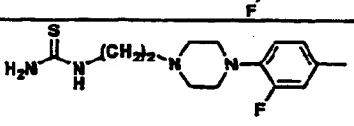
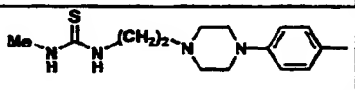
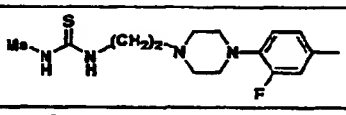
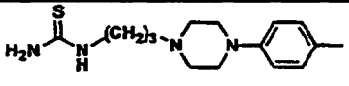
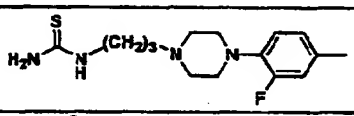
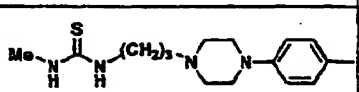
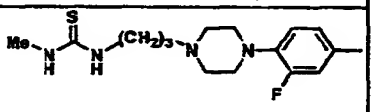
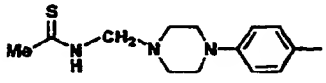
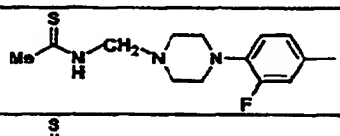
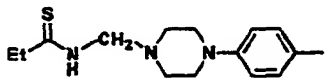
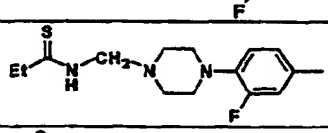
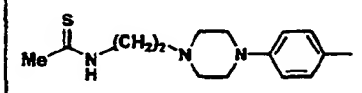
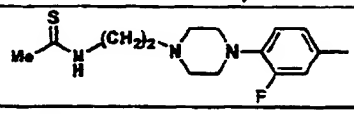
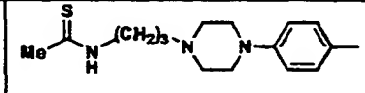
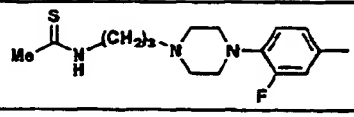
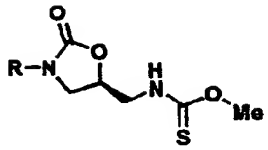
247		248	
249		250	
251		252	
253		254	
255		256	
257		258	
259		260	
261		262	
263		264	
265		266	
267		268	
269		270	
271		272	



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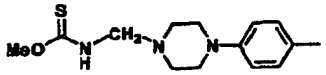
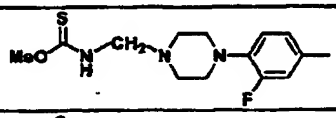
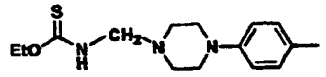
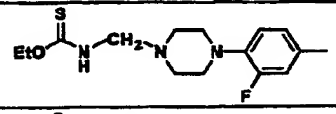
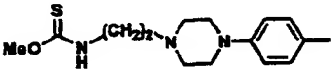
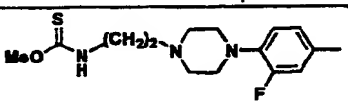
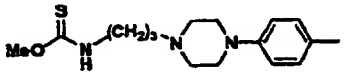
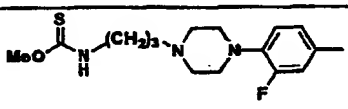
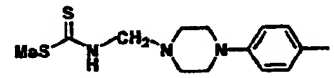
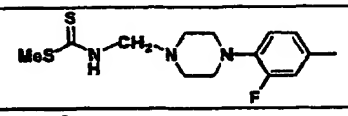
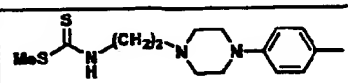
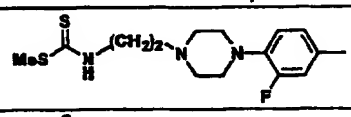
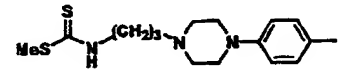
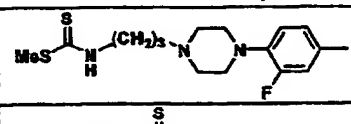
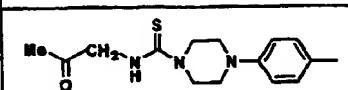
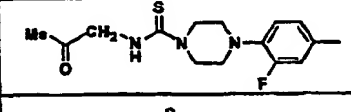
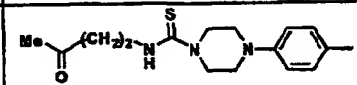
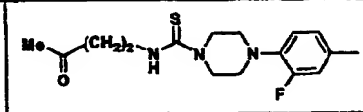
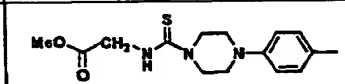
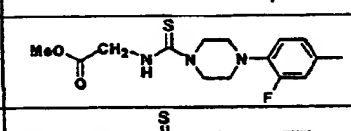
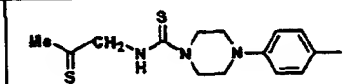
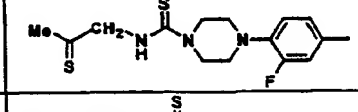
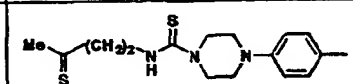
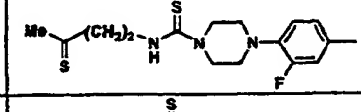
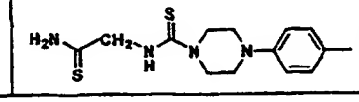
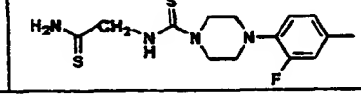
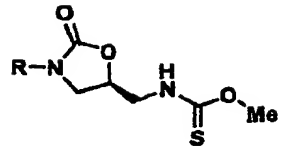
273		274	
275		276	
277		278	
279		280	
281		282	
283		284	
285		286	
287		288	
289		290	
291		292	
293		294	
295		296	
297		298	



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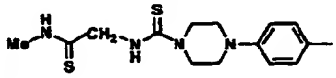
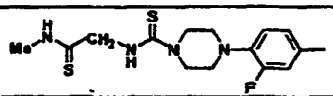
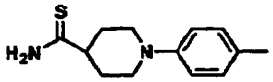
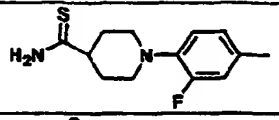
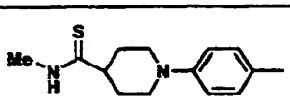
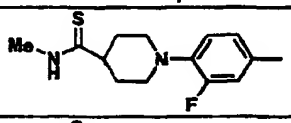
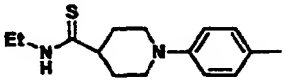
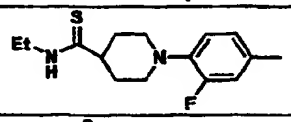
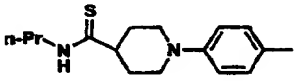
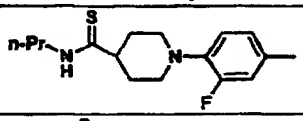
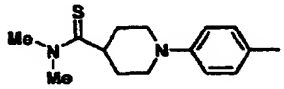
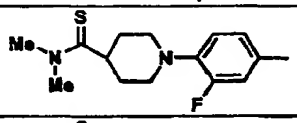
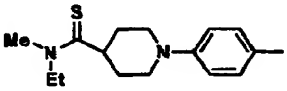
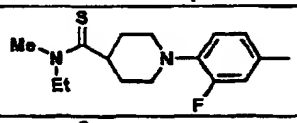
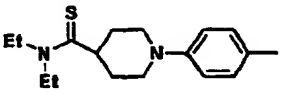
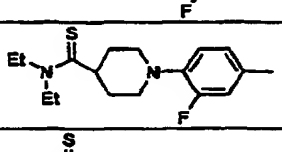
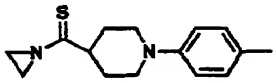
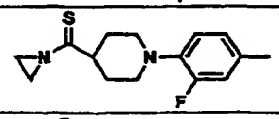
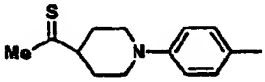
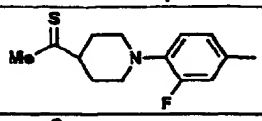
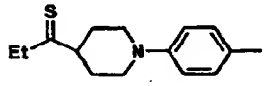
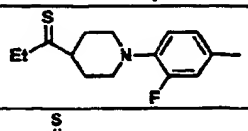
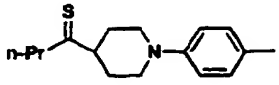
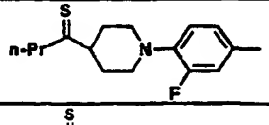
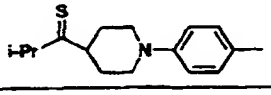
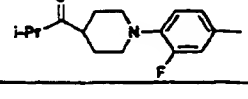
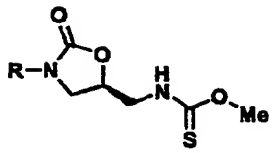
299		300	
301		302	
303		304	
305		306	
307		308	
309		310	
311		312	
313		314	
315		316	
317		318	
319		320	
321		322	
323		324	



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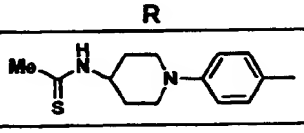
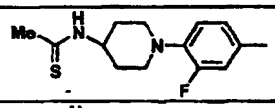
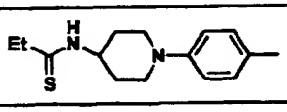
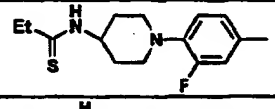
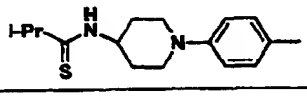
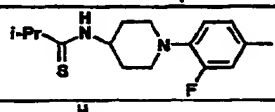
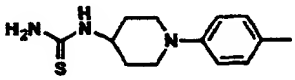
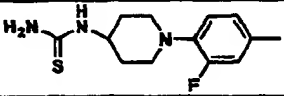
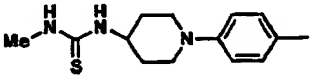
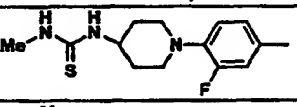
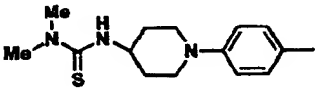
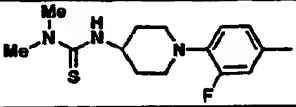
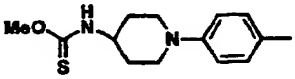
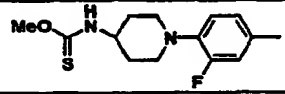
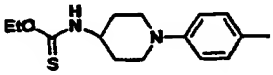
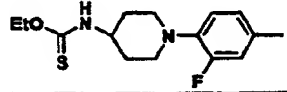
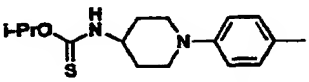
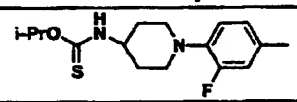
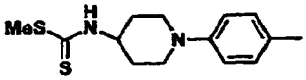
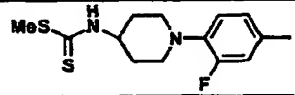
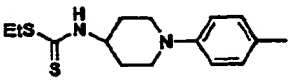
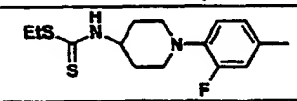
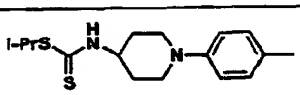
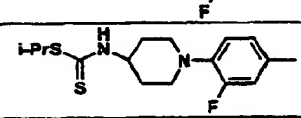
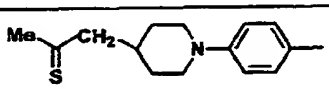
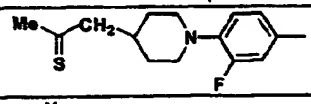
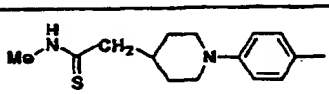
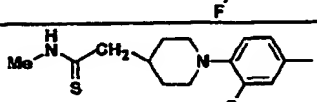
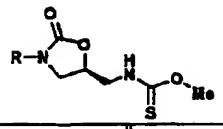
325		326	
327		328	
329		330	
331		332	
333		334	
335		336	
337		338	
339		340	
341		342	
343		344	
345		346	
347		348	
349		350	
351		352	



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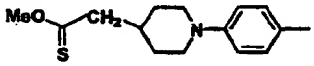
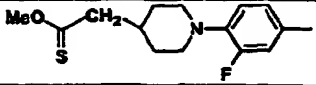
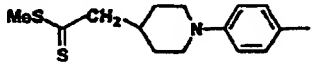
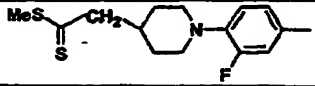
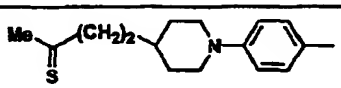
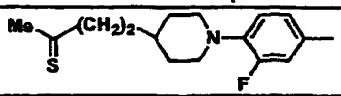
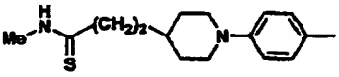
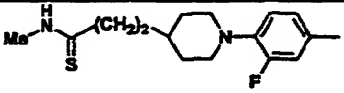
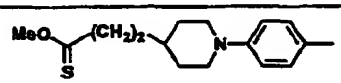
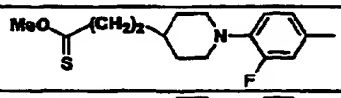
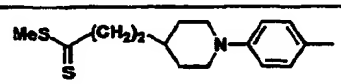
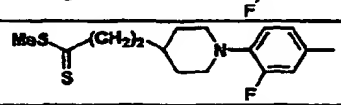
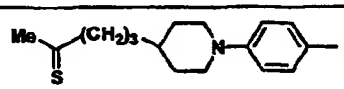
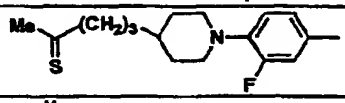
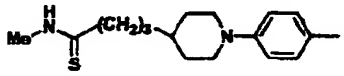
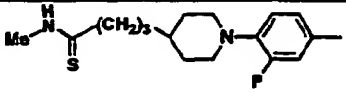
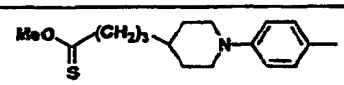
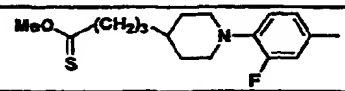
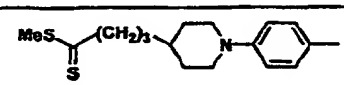
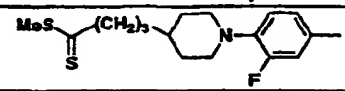
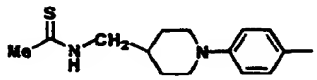
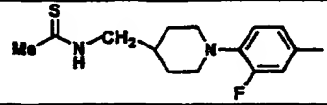
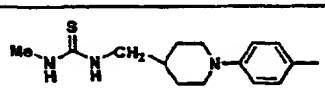
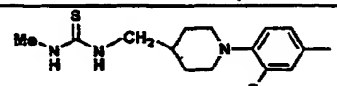
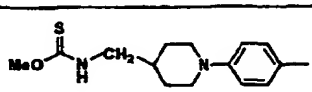
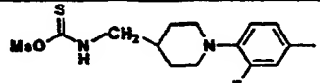
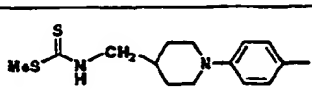
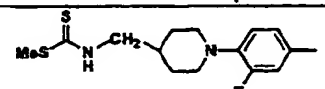
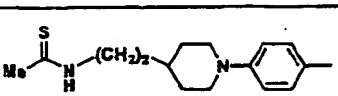
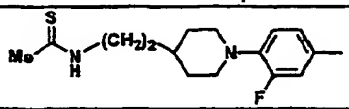
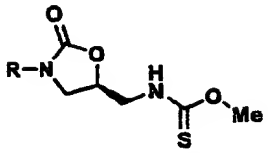
353		354	
355		356	
357		358	
359		360	
361		362	
363		364	
365		366	
367		368	
369		370	
371		372	
373		374	
375		376	
377		378	
379		380	
381		382	



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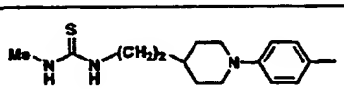
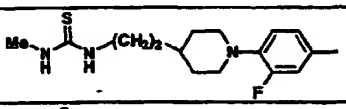
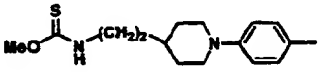
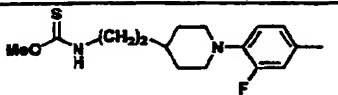
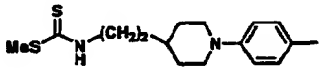
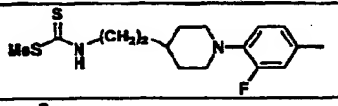
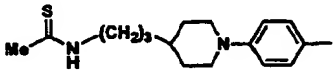
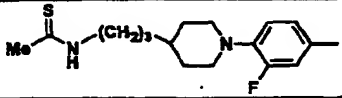
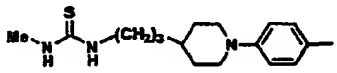
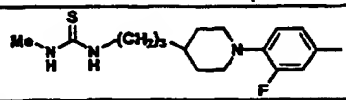
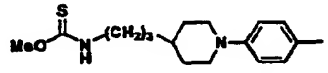
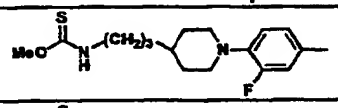
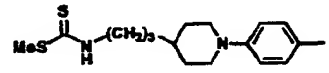
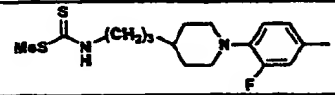
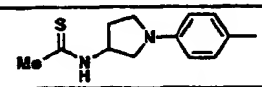
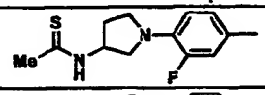
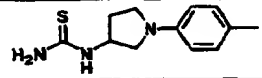
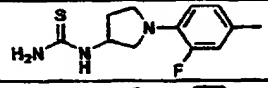
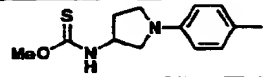
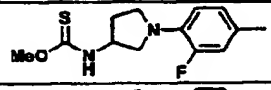
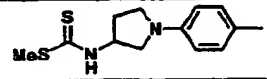
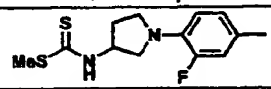
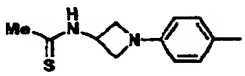
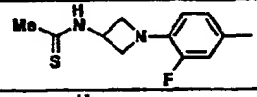
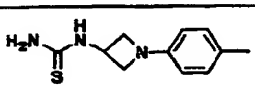
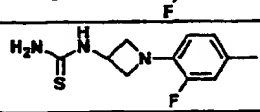
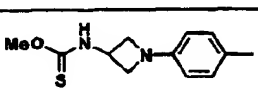
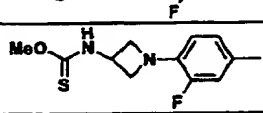
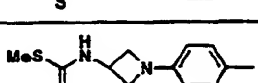
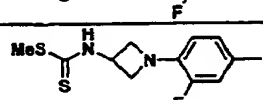
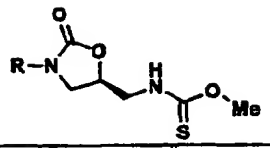
383		384	
385		386	
387		388	
389		390	
391		392	
393		394	
395		396	
397		398	
399		400	
401		402	
403		404	
405		406	
407		408	
409		410	
411		412	



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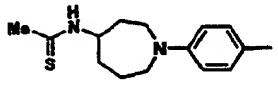
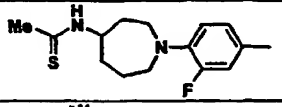
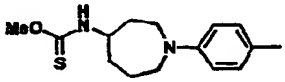
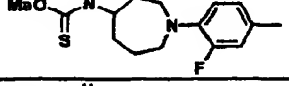
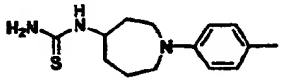
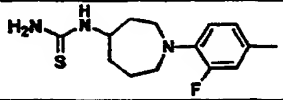
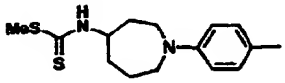
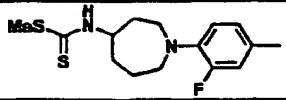
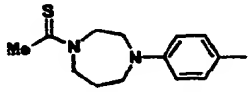
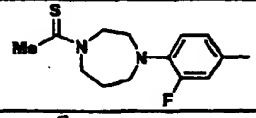
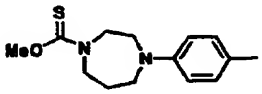
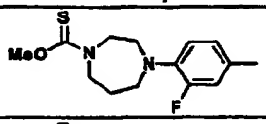
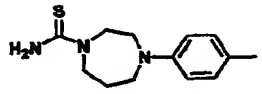
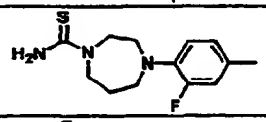
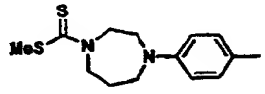
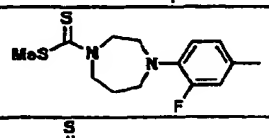
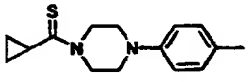
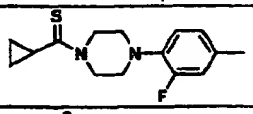
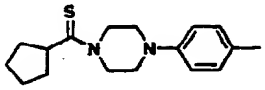
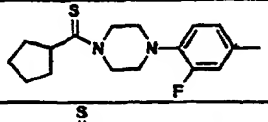
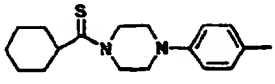
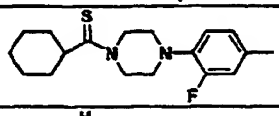
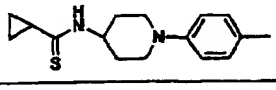
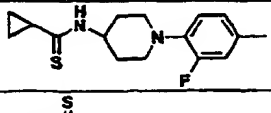
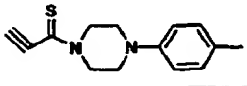
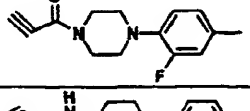
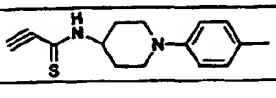
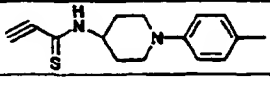
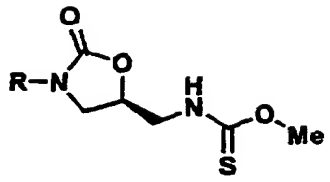
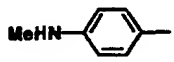
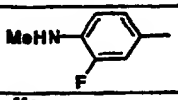
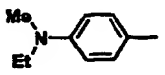
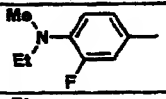
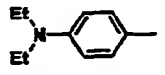
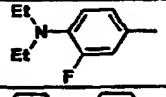
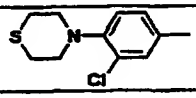
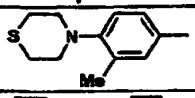
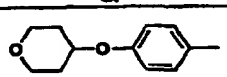
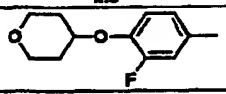
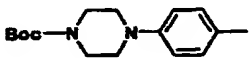
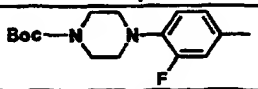
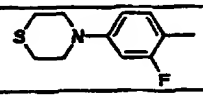
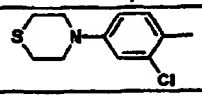
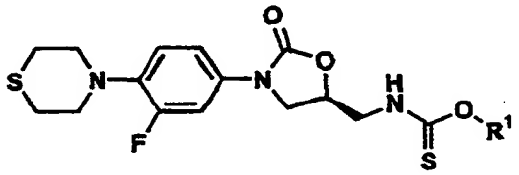
413		414	
415		416	
417		418	
419		420	
421		422	
423		424	
425		426	
427		428	
429		430	
431		432	
433		434	
435		436	
437		438	
439		440	



No.	R	No.	R
441		442	
443		444	
445		446	
447		448	
449		450	
451		452	
453		454	



No.	R^1	No.	R^1
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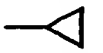
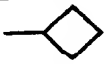
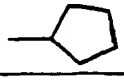
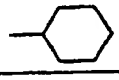
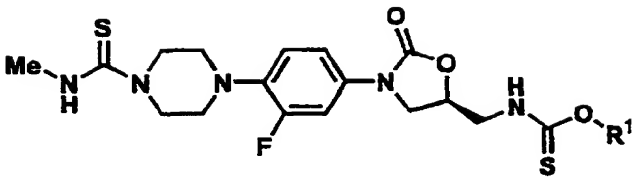
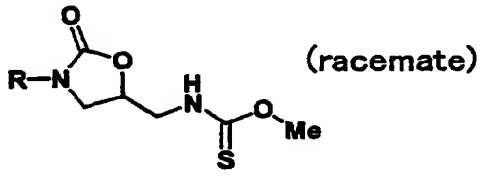
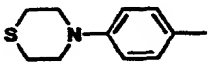
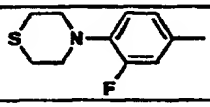
457	i-Pr	458	n-Bu
459	i-Bu	460	tert-Bu
461	n-Pent	462	n-Hex
463		464	
465		466	



No.	R^1	No.	R^1
467	Et	468	n-Pr

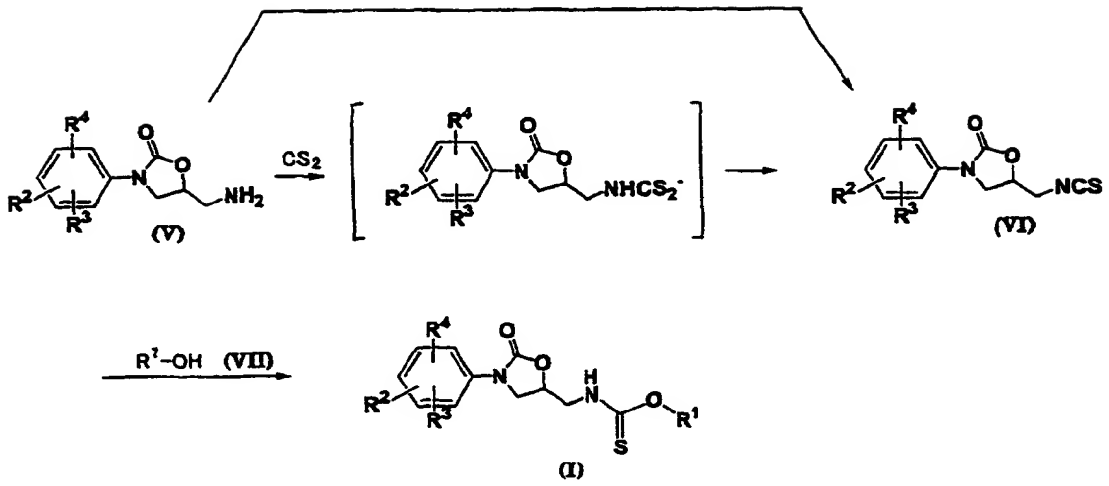


(racemate)

No.	R	No.	R
469		470	

[0022] The thiocarbamic acid derivatives of the present invention which are represented by the aforementioned general formulas (I) to (IV) can be prepared, for example, by the following method. However, the preparation methods of the aforementioned compounds are not limited thereto. In the following preparation methods, specific explanations will be given as for the compounds represented by the aforementioned general formula (I), and it is obvious that these preparation methods include the compounds represented by the aforementioned general formulas (II) to (IV). In addition, specific and detailed explanations will be given in the examples of the present specification as for preparations of typical compounds of the thiocarbamic acid derivatives of the present invention. Accordingly, persons skilled in the art can readily prepare the compounds of the present invention which are encompassed within the aforementioned general formula (I) by referring to the following general explanation and specific explanation in the examples, appropriately choosing starting materials, reagents, and reaction conditions, and if necessary, suitably modifying or altering these methods.

[0023] The first preparation method of the compounds of the present invention include a method which involves the use of a compound represented by the general formula (V) as a starting material and synthesis of the thiocarbamic acid derivative represented by the general formula (I) via a novel compound represented by the general formula (VI):



wherein R^1, R^2, R^3 and R^4 have the same meanings as those defined above.

[0024] In this method, the compound represented by the general formula (VI) can be prepared by reacting the compound represented by the general formula (V) with carbon disulfide in the presence of a base such as triethylamine in a solvent such as tetrahydrofuran, and reacting the resulting dithiocarbamate with ethyl chlorocarbonate, copper sulfate, iron nitrate, iron sulfate, zinc sulfide or other reagent at a temperature ranging from ice-cooling temperature to 200°C. As other preparation methods, the compound represented by the general formula (VI) can directly be synthesized by a preparation method which comprises the step of reacting the compound represented by the general formula (V) with thiophosgene in the presence of a base such as triethylamine in a solvent such as tetrahydrofuran, and by a method disclosed in Organic Synthesis Collective Volume, Vol. 1, p.447.

[0025] Then, the compound represented by the general formula (I) can be prepared by reacting the compound represented by the general formula (VI) with the compound represented by the general formula (VII) in the presence or absence of a base without solvent or in a solvent.

[0026] As the solvent used in the aforementioned reaction, any solvents may be used so far that they do not inhibit the reaction. Examples include aprotic polar solvents such as acetone, acetonitrile, N,N-dimethylformamide, N-methyl-2-pyrrolidone, dimethylsulfoxide, tetramethylene sulfone, tetramethylene sulfoxide, and hexamethylphosphoric triamide; etheric solvents such as diethyl ether, diisopropyl ether, and tetrahydrofuran; ester solvents such as methyl acetate and ethyl acetate; aromatic hydrocarbon solvents such as benzene and toluene; organic base solvents such as pyridine, picoline, lutidine, and collidine; halogenated hydrocarbon solvents such as dichloromethane, 1,2-dichloroethane, and chloroform; and mixtures thereof. Examples of the base include inorganic bases such as lithium, sodium, sodium hydride, potassium, potassium tert-butoxide, potassium carbonate, sodium carbonate, and sodium hydrogencarbonate; and organic bases such as triethylamine and diisopropylethylamine. The reaction is carried out at a temperature ranging from an ice-cooling temperature to 200°C.

[0027] The second preparation method of the compounds of the present invention includes a method comprising the step of reacting the compound represented by the general formula (V) with an appropriate O-alkyl chlorothiocarbonate in the presence of a base such as triethylamine in a solvent such as tetrahydrofuran at a temperature ranging from an ice-cooling temperature to a refluxing temperature of a solvent to obtain the compound of the general formula (I).

[0028] In the third preparation method of the compounds of the present invention, a compound represented by the general formula (I), wherein any one of R^2, R^3 and R^4 is a cycloalkyloxy group having a heteroatom as a ring constituting atom or a saturated heterocyclic group and wherein said group has a protected nitrogen atom, may be subjected to deprotection of the nitrogen to prepare the corresponding deprotected compound of the general formula (I).

[0029] The deprotection can be carried out by various methods depending on the type of a protecting group for the nitrogen atom. For example, when the protecting group is an amide-type protecting group such as an alkanoyl group and an arylcarbonyl group, the deprotection may be carried out by hydrolysis using an acid or a base to prepared the desired compound. The hydrolysis of the amide may be carried out by a known method. In acidic hydrolysis, an acid such as hydrochloric acid, sulfuric acid, and trifluoroacetic acid may be used, and in basic hydrolysis, a base such as sodium hydroxide and potassium hydroxide may be used. These acids or bases may be used as aqueous solutions. The deprotection may be carried out in an organic solvent including alcoholic solvents such as methanol, ethanol, n-butanol, sec-butanol, and tert-butanol; etheric solvents such as diethyl ether, diisopropyl ether, and tetrahydrofuran;

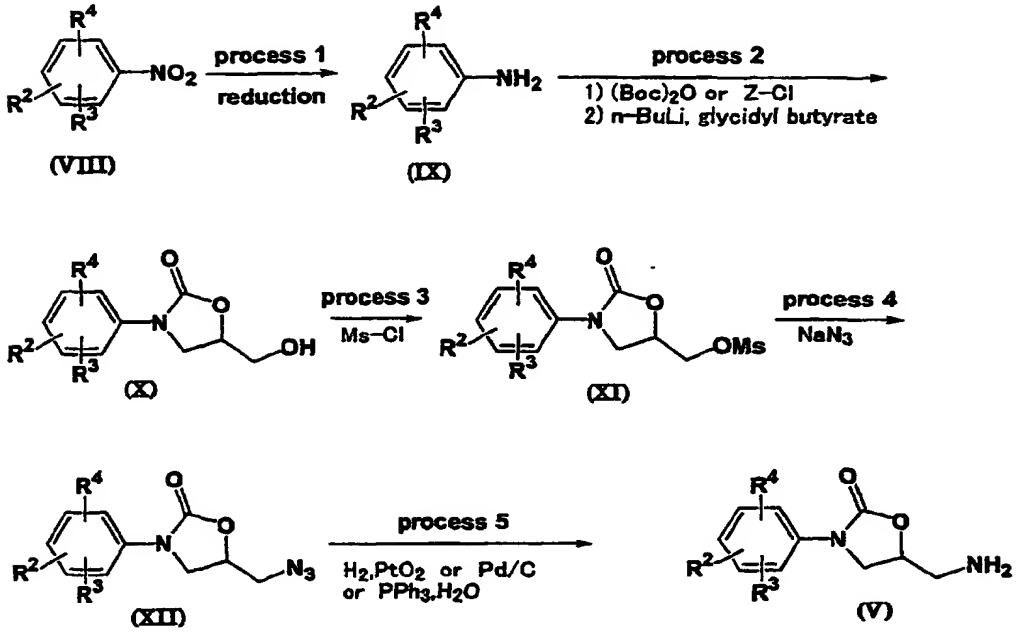
and ester solvents such as methyl acetate and ethyl acetate, or in a water-containing organic solvent at a temperature ranging from room temperature to a refluxing temperature of a solvent. When the protecting group is an urethane-type protecting group such as a lower alkoxycarbonyl group, the deprotection can be carried out by treatment with an acid such as hydrochloric acid, hydrobromic acid, and trifluoroacetic acid without a solvent or in a solvent such as acetic acid, ethyl acetate, 1,4-dioxane, water, methanol, ethanol, and a mixture thereof at a temperature ranging from an ice-cooling temperature to 200°C to prepare the desired compound.

[0030] In the forth preparation method of the present invention, the compound of the general formula (I) obtained in the third preparation method wherein any one of R^2, R^3 and R^4 is a cycloalkyloxy group having a heteroatom as a ring constituting atom or a saturated heterocyclic group and wherein said group has a deprotected nitrogen atom can be subjected to appropriate alkylation, acylation, urethane-introduction, urea-introduction, thioacylation, thiourea-introduction, thiocarbamation or other reaction; or the compound can be subjected to an appropriate reaction such as acylation and urethane-introduction, and then the resulting carbonyl group can be converted into a thiocarbonyl group by using the Lawesson's reagent or other reagent, to obtain the corresponding compound of general formula (I) wherein the nitrogen atom is substituted.

[0031] The introduction of a substituent into the nitrogen atom can be carried out by various methods depending upon the kind of the substituent. For example, for alkylation, alkylation using an alkyl halide, alkyl sulfonate, or other reagent, or the Michael addition using an acrylic acid ester or other reagent can be carried out in the presence or absence of a base without a solvent or in a solvent to obtain the corresponding compound of the general formula (I). Alternatively, acylation or urethane-introduction using an acyl halide and the like; urea-introduction using sodium cyanate and the like; thioacylation using a thioacyl halide and the like; thiourea-introduction using an alkylisothiocyanate and the like; or thiocarbamation using an O-alkyl chlorothiocarbonate and the like can be carried out in the presence of a base without a solvent or in a solvent, and if necessary, conversion of the carbonyl group of the compound having a nitrogen atom substituted with an acyl group or the like into thiocarbonyl group can be carried out using the Lawesson's reagent without a solvent or in a solvent to obtain the corresponding compound of the general formula (I).

[0032] As for the solvents used in these reactions, any solvents may be used so far that they do not inhibit the reactions. Examples include water; alcoholic solvents such as methanol and ethanol; aprotic polar solvents such as acetone, acetonitrile, N,N-dimethylformamide, N-methyl-2-pyrrolidone, dimethylsulfoxide, tetramethylene sulfone, tetramethylene sulfoxide, and hexamethylphosphoric triamide; etheric solvents such as diethyl ether, diisopropyl ether, and tetrahydrofuran; ester solvents such as methyl acetate and ethyl acetate; aromatic hydrocarbon solvents such as benzene and toluene; organic acid solvents such as acetic acid; organic base solvents such as pyridine, picoline, lutidine, and collidine; halogenated hydrocarbon solvents such as dichloromethane, 1,2-dichloroethane, and chloroform; and mixtures thereof. The base includes, for example, inorganic bases such as lithium, sodium, potassium, potassium tert-butoxide, potassium carbonate, sodium carbonate, and sodium hydrogencarbonate; and organic bases such as triethylamine and diisopropylethylamine. The reaction is carried out at a temperature ranging from an ice-cooling temperature to 200°C.

[0033] Some of the compounds represented by the general formulas (V) which are used as starting materials for the preparation methods of the compounds of the present invention are known compounds, which are disclosed in Japanese Patent Unexamined Publication No.(Hei) 8-73455, Journal of Medicinal Chemistry, Vol. 39, p. 673 and 680 (1996) and the like, and can be prepared according to the method described therein. Several novel compounds can be prepared, for example, by the following method, and the details of the preparation will be described in reference examples:



wherein Boc represents tert-butoxycarbonyl group; Z represents benzyloxycarbonyl group; n-Bu represents n-butyl group; Ms represents mesyl group; Ph represents phenyl group; and R^2, R^3 and R^4 have the same meanings as those defined above.

[0034] In process 1, the compound of the general formula (IX) can be obtained by reducing the nitro group of the compound of the general formula (VIII) by an appropriate reducing method, for example, a hydrogenation reduction which is carried out by using a catalyst such as platinum oxide, Raney nickel, and palladium-carbon in a solvent such as ethyl acetate and methanol at a temperature ranging from room temperature to 50°C under hydrogen pressure ranging from normal pressure to 50 atm; a reduction which is carried out by using iron powder and hydrochloric acid, acetic acid or another reagent; or other reducing method.

[0035] In process 2, the compound of the general formula (X) can be obtained by subjecting the amino group of the compound of the general formula (IX) to appropriate urethane-introduction, for example, using di-tert-butyl dicarbonate in an appropriate organic solvent such as methanol and tetrahydrofuran at a temperature ranging from an ice-cooling temperature to a refluxing temperature of a solvent; or using benzyloxycarbonyl chloride in the presence of a bas such as triethylamine, potassium carbonate, sodium carbonate, and sodium hydrogencarbonate in a solvent such as water; an organic solvent including acetone, methanol, and tetrahydrofuran; and a mixed solvent thereof at a temperature ranging from an ice-cooling temperature to a refluxing temperature of a solvent; then treating the resulting compound with a base such as n-butyllithium in an appropriate aprotic organic solvent such as tetrahydrofuran and N,N-dimethylformamide at a temperature ranging from -78°C to room temperature, and then reacting the resulting compound with glycidyl butylate.

[0036] In process 3, the compound of the general formula (XI) can be obtained by reacting the compound of the general formula (X) with methanesulfonyl chloride in the presence of a base such as triethylamine in an appropriate organic solvent such as dichloromethane and tetrahydrofuran at a temperature ranging from an ice-cooling temperature to a refluxing temperature of a solvent.

[0037] In process 4, the compound of the general formula (XII) can be obtained by reacting the compound of the general formula (XI) with sodium azide in an appropriate organic solvent such as tetrahydrofuran and N,N-dimethylformamide at a temperature ranging from an ice-cooling temperature to a refluxing temperature of a solvent.

[0038] In the compound of the general formula (XI), when any one of R^2, R^3 and R^4 has a protected nitrogen atom in the substituent, deprotection may be carried out in accordance with the third preparation method of the compound of the present invention after the azidation in process 4, and then if necessary, appropriate alkylation, acylation, urethane-introduction, thioacylation, thiourea-introduction, thiocarbamation or other reaction may be carried out in accordance with the forth preparation method to obtain the respective corresponding compounds of the general formula (XII).

[0039] In the compound of the general formula (XI), when any one of R^2, R^3 and R^4 is thiomorpholinyl group, the sulfur atom may be subjected to appropriate oxidation for conversion into S-oxide or S,S-dioxide, and then the corre-

sponding compound represented by the general formula (XII) can be prepared according to the process 4.

[0040] The oxidation of the sulfur atom can be carried out by various methods depending on target compounds. The conversion into S-oxide group can be carried out, for example, by using an oxidizing agent such as chromic acid, hydrogen peroxide, metachloroperbenzoic acid, sodium metaperiodate, and potassium metaperiodate in a solvent such as water, an organic solvent including tetrahydrofuran, methanol, acetonitrile, acetone, and dichloromethane, and a mixed solvent thereof at a temperature ranging from an ice-cooling temperature to a refluxing temperature of a solvent. The conversion into S,S-dioxide group can be carried out, for example, by using an oxidizing agent such as chromic acid, hydrogen peroxide, metachloroperbenzoic acid, osmium tetraoxide, and ruthenium tetraoxide in a solvent such as water, an organic solvent including tetrahydrofuran, methanol, acetone, and dichloromethane, and a mixed solvent thereof at a temperature ranging from an ice-cooling temperature to a refluxing temperature of a solvent.

[0041] In process 5, the compound represented by the general formula (V) can be obtained by reducing the azide group of the compound of the general formula (XII) by an appropriate reducing method, for example, a hydrogenation reduction which is carried out by using a catalyst such as platinum oxide and palladium carbon in a solvent such as methanol at a temperature ranging from room temperature to 50°C under hydrogen pressure ranging from normal pressure to 50 atom; a reducing method which is carried out by using triphenylphosphine and water in a solvent such as tetrahydrofuran at a temperature ranging from an ice-cooling temperature to a refluxing temperature of a solvent or other reducing method.

[0042] The medicament of the present invention is characterized to comprise the thiocarbamic acid derivative represented by the aforementioned general formulas (I) to (IV) or a salt thereof as an active ingredient. As the active ingredient of the medicament of the present invention, a substance selected from the group consisting of the aforementioned compound in free form and a pharmacologically acceptable salt thereof, and any crystal form thereof, a solvate thereof, and a hydrate thereof can be used, and two or more substances may be used in combination. As the medicament of the present invention, the aforementioned substance may be used *per se*. In general, the medicament is desirably provided in a form of a pharmaceutical composition which comprises the aforementioned substance as an active ingredient and one or more pharmaceutical additives.

[0043] The form of the pharmaceutical composition is not particularly limited, and the composition can be prepared, for example, as an oral preparation in the forms of capsules, tablets, fine granules, granules, powders, syrups and the like, or as a parenteral preparation in the forms of injections, suppositories, eye drops, eye ointments, ear drops, nasal drops, transdermal and transmucosal agents, inhalations, dermatologic preparation and the like. These preparations can be manufactured according to conventional methods after the addition of pharmacologically and pharmaceutically acceptable additives. For oral preparations and suppositories, pharmaceutical ingredients such as excipients such as lactose, D-mannitol, corn starch, and crystalline cellulose; disintegrators such as carboxymethylcellulose and carboxymethylcellulose calcium; binders such as hydroxypropyl cellulose, hydroxypropyl methylcellulose, and polyvinylpyrrolidone; lubricants such as magnesium stearate and talc; coating agents such as hydroxypropyl methylcellulose, sucrose, and titanium oxide; plasticizers such as poly(ethylene glycol); bases such as poly(ethylene glycol) and hard fat and the like may be used. For injections, eye drop, ear drop, or nasal drop, pharmaceutical ingredients including solubilizers or solubilizing aids which may constitute aqueous dosage forms or forms dissolved upon use such as distilled water for injection, physiological saline, and propylene glycol; pH modifiers such as inorganic or organic acids or bases; isotonicities such as sodium chloride, glucose, and glycerin; stabilizers and the like may be used. For eye ointments and dermatologic preparations, pharmaceutical ingredients which are suitable for ointments, creams, and patches such as white vaseline, macrogols, glycerin, liquid paraffin, and cotton cloth may be used.

[0044] The medicament of the present invention can be administered, for example, as an antibacterial agent for therapeutic or preventive treatment of infectious diseases of mammals including humans. A dose of the medicament of the present invention is not particularly limited, and an appropriate dose can be chosen depending on the kind of pathogenic bacteria, the age and body weight of a patient, severity of a disease and the like. For example, a daily dose is usually from about 10 to 2,000 mg for oral administration, and from about 1 to 1,000 mg for parenteral administration for an adult. The aforementioned dose can be administered once a day or several times a day as divided portions. However, it is desirable that the dose is suitably increased or decreased depending on purpose of therapeutic or preventive treatment, a body part suffering from infection, the kind of pathogenic bacteria, the age or symptom of a patient and the like.

Examples

[0045] The present invention will be explained by referring to Reference examples and Working Examples. However, the scope of the present invention is not limited to these examples. The abbreviations in the tables have the following meanings: Me: methyl group; Et: ethyl group; n-Pr: n-propyl group; i-Pr: i-propyl group; n-Bu: n-butyl group; Boc: tert-butoxycarbonyl group; Z: benzyloxycarbonyl group; Ms: mesyl group; cyc-Hex: cyclohexyl group; Ph: phenyl group.

Reference example 1

[0046] N-tert-Butoxycarbonyl-4-piperidinol

[0047] To a suspension of 50.0 g of 4-piperidinol in 250 ml of dried tetrahydrofuran, 125 ml of di-tert-butyl dicarbonate was added under ice-cooling and with stirring, and the mixture was stirred at room temperature for 30 minutes. After the reaction was completed, the solvent was evaporated under reduced pressure to obtain 120.5 g of a pale yellow liquid.

NMR spectrum ($CDCl_3$) δ ppm:
1.46(9H,s),1.47-1.50(2H,m),1.81-1.87(2H,m),3.01-3.10(2H,m),3.73-3.87(3H,m)
IR spectrum ν (liq.) cm^{-1}: 1698,3684
Mass spectrum (m/z) : 201(M^+)

[0048] The compound of Reference example 2 was obtained in the same manner as in Reference example 1.

Reference example 2

[0049] N-tert-Butoxycarbonyl-3-azetidinol
Appearance : yellow liquid
NMR spectrum (DMSO-d_6) δ ppm :
1.37(9H,s),3.55-3.60(2H,m),3.95-4.00(2H,m),4.30-4.40(1H,m),5.50(1H,d,J=6Hz)
IR spectrum ν (liq.) cm^{-1}: 1678,3416

Reference example 3

[0050] N-tert-Butoxycarbonyl-4-methoxypiperidine

[0051] To a suspension of 8.77 g of 60% sodium hydride in 300 ml of dried N,N-dimethylformamide, a solution of 49.0 g of N-tert-butoxycarbonyl-4-piperidinol in 190 ml of dried N,N-dimethylformamide was added under stirring at room temperature. Then, the mixture was added dropwise with 30.4 ml of methyl iodide, and stirred at the same temperature for 5 hours. The reaction solution was poured into ice water, and extracted with ethyl acetate. The extract was washed with saturated brine and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate : n-heptane = 1 : 2 to 1 : 1) to obtain 44.1 g of a colorless liquid.

NMR spectrum ($CDCl_3$) δ ppm :
1.45-1.55(2H,m),1.46(9H,s),1.80-1.90(2H,m),3.05-3.15(2H,m),3.30-3.40(1H,m),3.35(3H, s),3.70-3.80(2H,m)
IR spectrum ν (liq.) cm^{-1}: 1698
Mass spectrum (m/z) : 215 (M^+)

Reference example 4

[0052] N-tert-Butoxycarbonyl-3-(2-methoxyethoxy)azetidine

[0053] To a suspension of 0.25 g of 60% sodium hydride in 5 ml of dried N,N-dimethylformamide, a solution of 1.00 g of N-tert-butoxycarbonyl-3-azetidinol in 3 ml of dried N,N-dimethylformamide was added under stirring at room temperature. The mixture was stirred at room temperature for 30 minutes, then added dropwise with a solution of 0.98 g of 2-methoxyethyl methanesulfonate in 2 ml of dried N,N-dimethylformamide, and stirred at the same temperature for 4 hours. The reaction solution was poured into ice water, and extracted with ethyl acetate. The extract was washed successively with water and saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate : n-heptane = 1 : 3) to obtain 0.67 g of a colorless liquid.

NMR spectrum (DMSO-d_6) δ ppm :
1.37(9H,s),3.25(3H,s),3.41-3.45(2H,m),3.46-3.49(2H,m),3.64(2H,dd,J=9,4Hz),3.98(2H,d d,J=9,6.5Hz),4.21-4.26(1H, m)
IR spectrum ν (liq.) cm^{-1}: 1706

Reference example 5

[0054] 4-Methoxypiperidine hydrochloride

[0055] To 220ml of 9 % hydrogen chloride ethyl acetate solution, a solution of 43.9 g of N-tert-butoxycarbonyl-4-methoxypiperidine in 220 ml of ethyl acetate was added under ice-cooling and with stirring, and the mixture was stirred under ice-cooling for 2.5 hours. After the reaction, the precipitated crystals were collected by filtration to obtain 29.1 g

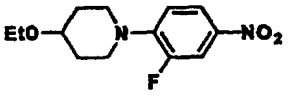
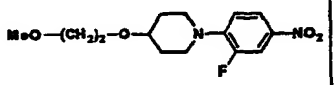
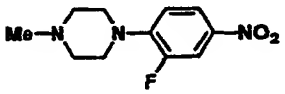
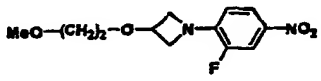
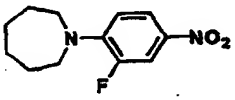
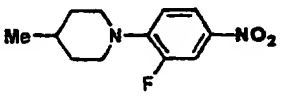
of colorless crystals.
NMR spectrum ($CDCl_3$) δ ppm :
1.95-2.05(2H,m),2.10-2.20(2H,m),3.15-3.30(4H,m),3.33(3H,s),3.50-3.60(1H,m)
IR spectrum ν (liq.) cm^{-1}: 3448
Mass spectrum (m/z) : 115(M^+)
[0056] The compound of Reference example 6 was obtained in the same manner as in Reference example 5.

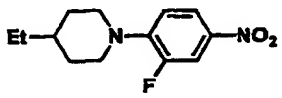
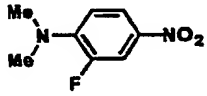
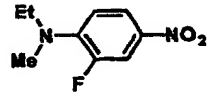
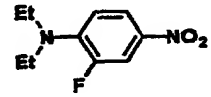
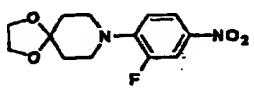
Reference example 6

[0057] 3-(2-Methoxyethoxy)azetidine hydrochloride
Appearance : pale yellow liquid
NMR spectrum (DMSO-d_6) δ ppm :
3.26(3H,s),3.43(2H,t,J=4.5Hz),3.54(2H,t,J=4.5Hz),3.75-3.80(2H,m),4.05-4.10(2H,m),4. 35-4.40(1H,m)
IR spectrum ν (liq.) cm^{-1}: 3436
Mass spectrum (m/z) : 131(M^+)

Reference example 7

[0058] 3-Fluoro-4-(4-methoxypiperidin-1-yl)nitrobenzene
[0059] To a solution of 15.0 g of 3,4-difluoronitrobenzene and 41 ml of N,N-diisopropylethylamine in 150 ml of dried acetonitrile, 15.8 g of 4-methoxypiperidine hydrochloride was added, and the mixture was heated under reflux for 5 hours. Th solvent was evaporated under reduced pressure, the residue was added with water and 10% aqueous sodium hydroxide, and the resulting alkaline mixture was extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure to obtain 24.1 g of a yellowish brown liquid.
NMR spectrum (DMSO-d_6) δ ppm :
1.54-1.62(2H,m),1.92-2.00(2H,m),3.08-3.16(2H,m),3.28(3H,s),3.38-3.46(1H,m),3.49-3.5 7(2H,m),7.16(1H,t,J=8.5Hz), 7.95(1H,dd,J=14,3Hz),7.97(1H,dd,J=8.5,3Hz)
IR spectrum ν (liq.) cm^{-1}: 1336,1518
Mass spectrum (m/z): 254(M^+)
[0060] The compounds of Reference examples 8 through 18 were obtained in the same manner as in Reference example 7.

Reference example		Physical properties [recrystallization solvent]
8		yellow needles [i-PrOH] mp,62～63℃ Elemental analysis for $C_{13}H_{17}FN_2O_3$ Calcd. % : C,58.20;H,6.39;N,10.44 Found % : C,58.10;H,6.60;N,10.45
9		yellow crystals [i-Pr_2O-n-Heptane] mp,58.5～59.5℃ Elemental analysis for $C_{14}H_{19}FN_2O_4$ Calcd. % : C,56.37;H,6.42;N,9.39 Found % : C,56.36;H,6.54;N,9.34
10		yellowish brown prisms [i-Pr_2O] mp,68～68.5℃ Elemental analysis for $C_{11}H_{14}FN_3O_2$ Calcd. % : C,55.22;H,5.90;N,17.56 Found % : C,55.24;H,5.71;N,17.63
11		yellow liquid NMR(DMSO-d_6) δ ppm:3.27(3H,s),3.47(2H,t,J=4.5Hz),3.56(2H,t,J=4.5Hz),3.95-4.00(2H,m),4.35-4.40(2H,m),4.45-4.50(1H,m),6.57(1H,t,J=9Hz),7.89(1H,dd,J=13,2.5Hz),7.93(1H,dd,J=9,2.5Hz) IR ν (liq.) cm^{-1}:1326,1532 MS(m/z):270(M^+)
12		yellowish brown liquid NMR(DMSO-d_6) δ ppm:1.50-1.60(4H,m),1.70-1.85(4H,m),3.55-3.65(4H,m),6.96(1H,t,J=9Hz),7.88(1H,dd,J=16,3Hz),7.90(1H,dd,J=9,3Hz) IR ν (liq.) cm^{-1}:1324,1522 MS(m/z):238(M^+)
13		yellowish brown liquid NMR(DMSO-d_6) δ ppm:0.95(3H,d,J=6Hz),1.20-1.35(2H,m),1.55-1.65(1H,m),1.65-1.80(2H,m),2.85-3.00(2H,m),3.60-3.75(2H,m),7.13(1H,t,J=9Hz),7.93(1H,dd,J=13.5,2.5Hz),7.97(1H,dd,J=9,2.5Hz) IR ν (liq.) cm^{-1}:1334,1512 MS(m/z):238(M^+)

Reference example		Physical properties [recrystallization solvent]
14		yellowish brown liquid NMR($CDCl_3$) δ ppm:0.93(3H,t,J=7.5Hz),1.25-1.45(5H,m),1.82(2H,d,J=5.5Hz),2.86(2H,t,J=12Hz),3.71(2H,d,J=12Hz),6.91(1H,t,J=9Hz),7.88(1H,dd,J=13.5,2.5Hz),7.96(1H,dd,J=9,2.5Hz) IR ν (liq.) cm^{-1}:1338,1518 MS(m/z):252(M^+)
15		yellow needles[i-PrOH] mp,95~96℃ Elemental analysis for $C_8H_9FN_2O_2$ Calcd. % : C,52.17;H,4.93;N,15.21 Found % : C,51.93;H,4.72;N,15.21
16		yellow needles[n-Heptane] mp,40~41℃ Elemental analysis for $C_9H_{11}FN_2O_2$ Calcd. % : C,54.54;H,5.59;N,14.13 Found % : C,54.26;H,5.76;N,14.19
17		yellow prisms[n-Heptane] mp,49.5~50.5℃ Elemental analysis for $C_{10}H_{13}FN_2O_2$ Calcd. % : C,56.60;H,6.17;N,13.20 Found % : C,56.41;H,6.01;N,13.06
18		yellow needles[i-PrOH] mp,125~125.5℃ Elemental analysis for $C_{13}H_{15}FN_2O_4$ Calcd. % : C,55.32;H,5.36;N,9.92 Found % : C,55.21;H,5.18;N,9.88

Reference example 19

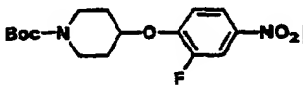
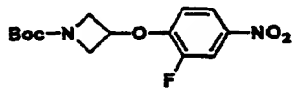
[0061] 3-Fluoro-4-(2-methoxyethoxy)nitrobenzene

[0062] To a suspension of 4.20 g of 60 % sodium hydride in 100 ml of dried tetrahydrofuran, a solution of 7.90 g of ethylene glycol monomethyl ether in 50 ml of dried tetrahydrofuran was added dropwise under ice-cooling and with stirring, and the mixture was stirred at room temperature for 15 minutes. The reaction mixture was added dropwise with a solution of 15.0 g of 3,4-difluoronitrobenzene in 50 ml of dried tetrahydrofuran under ice-cooling and with stirring, and stirred at the same temperature for 30 minutes. The reaction solution was added with ice water, and extracted with ethyl acetate. The extract was washed with saturated brine, and dri d over sodium sulfate, and then the solvent was

evaporated under reduced pressure. The residue was washed with n-hexane to obtain 19.0 g of yellow crystals. Recrystallization from diisopropyl ether gave yellow needles having the melting point of from 62.5 to 63°C.

Elemental analysis for $C_9H_{10}FNO_4$						
Calculated %	C,	50.24;	H,	4.68;	N,	6.51
Found %	C,	50.18;	H,	4.54;	N,	6.50

[0063] The compounds of Reference examples 20 through 21 were obtained in the same manner as in Reference example 19.

Reference example		Physical properties [recrystallization solvent]
20		pale yellow columns[i-PrOH] mp,91.5~93°C Elemental analysis for $C_{16}H_{21}FN_2O_5$ Calcd. % : C,56.46;H,6.22;N,8.23 Found % : C,56.36;H,6.34;N,8.29
21		pale yellow needles[EtOH] mp,117~117.5°C Elemental analysis for $C_{14}H_{17}FN_2O_5$ Calcd. % : C,53.84;H,5.49;N,8.97 Found % : C,53.73;H,5.44;N,8.97

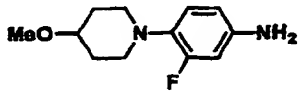
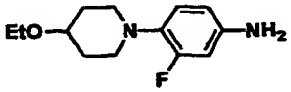
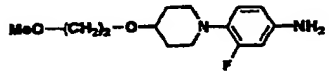
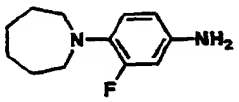
Reference example 22

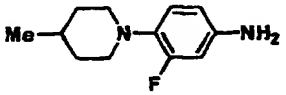
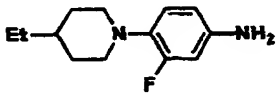
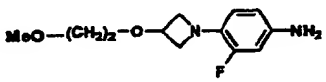
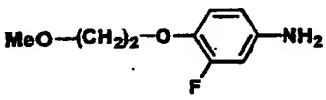
[0064] 3-Fluoro-4-(4-methylpiperazin-1-yl)aniline

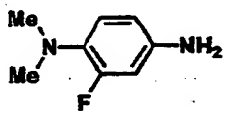
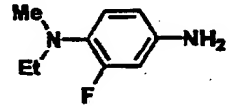
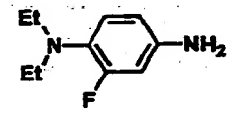
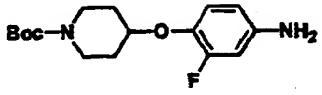
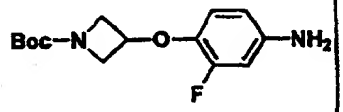
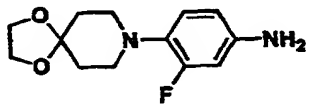
[0065] A suspension of 19.0 g of 3-fluoro-4-(4-methylpiperazin-1-yl)nitrobenzene and 0.190 g of platinum(IV) oxid in 190 ml of methanol was stirred at a hydrogen pressure of 2 atm at ordinary temperature for 2 hours. The catalyst was filtered off, and then the filtrate was concentrated under reduced pressure to obtain 17.0 g of dark brown crystals. Recrystallization from diisopropyl ether gave dark brown prisms having the melting point of from 87 to 88°C.

Elemental analysis for $C_{11}H_{16}FN_3$						
Calculated %	C,	63.13;	H,	7.71;	N,	20.08
Found %	C,	63.10;	H,	7.46;	N,	20.08

[0066] The compounds of Reference examples 23 through 36 were obtained in the same manner as in Reference example 22.

Reference example		Physical properties [recrystallization solvent]
23		black liquid NMR(DMSO-d_6) δ ppm:1.49-1.59(2H,m), 1.86-1.94(2H,m),2.59-2.67(2H,m),2.97-3.04(2H,m),3.22-3.29(1H,m),3.25(3H,s),4.83(2H,br-s),6.29(1H,dd,J=8.5,2.5Hz),6.33(1H,dd,J=14.5,2.5Hz),6.75(1H,t,J=8.5Hz) IR ν (liq.) cm^{-1}:3360,3448 MS(m/z):224(M^+)
24		blackish brown liquid NMR(DMSO-d_6) δ ppm:1.11(3H,t,J=7.5Hz),1.50-1.60(2H,m),1.85-1.95(2H,m),2.60-2.70(2H,m),2.95-3.05(2H,m),3.30-3.40(1H,m),3.47(2H,q,J=7.5Hz),4.83(2H,br-s),6.30(1H,dd,J=8.5,2.5Hz),6.30(1H,dd,J=14,2.5Hz),6.75(1H,dd,J=9.5,8.5Hz) IR ν (liq.) cm^{-1}:3360,3456 MS(m/z):238(M^+)
25		brown liquid NMR(DMSO-d_6) δ ppm:1.50-1.60(2H,m), 1.85-1.95(2H,m),2.60-2.65(2H,m),2.95-3.05(2H,m),3.26(3H,s),3.35-3.40(1H,m),3.44(2H,t,J=5Hz),3.54(2H,t,J=5Hz),4.83(2H,br-s),6.28(1H,dd,J=8.5,2.5Hz), 6.32(1H,dd,J=14.5,2.5Hz),6.75(1H,t,J=8.5Hz) IR ν (liq.) cm^{-1}:3364,3464 MS(m/z):268(M^+)
26		blackish purple liquid NMR(DMSO-d_6) δ ppm:1.50-1.65(4H,m), 1.65-1.75(4H,m),3.07(4H,t,J=6Hz),4.70(2H,br-s),6.26(1H,dd,J=8.5,2.5Hz),6.31(1H,dd,J=14.5,2.5Hz),6.71(1H,t,J=8.5Hz) IR ν (liq.) cm^{-1}:3224,3356 MS(m/z):208(M^+)

Reference example		Physical properties [recrystallization solvent]
27		black liquid NMR(DMSO-d_6) δ ppm:0.93(3H,d,J=6.5 Hz),1.20-1.30(2H,m),1.35-1.50(1H,m), 1.60-1.70(2H,m),2.45-2.60(2H,m),3.00-3.10(2H,m),4.81(2H,br-s),6.28(1H,dd,J =9,2.5Hz),6.32(1H,dd,J=14.5,2.5Hz),6.74(1H,t,J=9Hz) IR ν (liq.) cm^{-1}:3224,3356,3464 MS(m/z):208(M^+)
28		blackish brown liquid NMR($CDCl_3$) δ ppm:0.91(3H,t,J=7.5Hz), 1.15-1.30(1H,m),1.32(2H,quin,J=7.5Hz),1.38(1H,dd,J=12,4Hz),1.43(1H,dd,J =12,4Hz),1.76(2H,d,J=4Hz),2.56(2H,td,J=11.5,2Hz),3.26(2H,d,J=11.5Hz),3.34(2H,br-s),6.39(1H,dd,J=9,2.5Hz),6.42(1H,dd,J=13.5,2.5Hz),6.82(1H,t,J=9 Hz) IR ν (liq.) cm^{-1}:3352,3464 MS(m/z):222(M^+)
29		black liquid NMR(DMSO-d_6) δ ppm:3.25(3H,s),3.40-3.45(4H,m),3.50(2H,t,J=4.5Hz),3.90-4.00(2H,m),4.25-4.35(1H,m),4.61(2H,br-s),6.25-6.35(3H,m) IR ν (liq.) cm^{-1}:3360,3430 MS(m/z):240(M^+)
30		blackish brown liquid NMR($CDCl_3$) δ ppm:3.44(3H,s),3.49(2H, br-s),3.71(2H,t,J=5Hz),4.10(2H,t,J=5 Hz),6.30-6.40(1H,m),6.45(1H,dd,J=12.5,2.5Hz),6.84(1H,t,J=8.5Hz) IR ν (liq.) cm^{-1}:3368,3460 MS(m/z):185(M^+)

Reference example		Physical properties [recrystallization solvent]
31		pale green crystals NMR(DMSO-d_6) δ ppm:2.58(6H,s),4.79(2H,br-s),6.30(1H,dd,J=8.5,2.5Hz),6.33(1H,dd,J=14,2.5Hz),6.73(1H,t,J=8.5Hz) IR ν (KBr) cm^{-1}:3328,3456 MS(m/z):154(M^+)
32		blackish purple liquid NMR(DMSO-d_6) δ ppm:0.95(3H,t,J=7.5Hz),2.57(3H,s),2.88(2H,q,J=7.5Hz),4.82(2H,br-s),6.29(1H,dd,J=9,2.5Hz),6.32(1H,dd,J=16,2.5Hz),6.75(1H,t,J=9Hz) IR ν (liq.) cm^{-1}:3224,3348 MS(m/z):168(M^+)
33		grayish brown crystals NMR(DMSO-d_6) δ ppm:0.89(6H,t,J=7Hz),2.91(4H,q,J=7Hz),4.89(2H,br-s),6.25-6.35(2H,m),6.78(1H,t,J=9Hz) IR ν (KBr) cm^{-1}:3208,3332 MS(m/z):182(M^+)
34		dark brown liquid NMR(DMSO-d_6) δ ppm:1.40(9H,s),1.45-1.55(2H,m),1.75-1.85(2H,m),3.05-3.20(2H,m),3.55-3.70(2H,m),4.05-4.15(1H,m),4.90(2H,br-s),6.29(1H,ddd,J=8.5,2.5,1Hz),6.38(1H,dd,J=13.5,2.5Hz),6.84(1H,t,J=8.5Hz) IR ν (liq.) cm^{-1}:1682,3368 MS(m/z):310(M^+)
35		yellowish brown prisms [i-Pr_2O] mp,85.5~86℃ Elemental analysis for $C_{14}H_{19}FN_2O_3$ Calcd. % : C,59.56;H,6.78;N,9.92 Found % : C,59.43;H,7.06;N,9.89
36		dark brown needles [i-PrOH] mp,113.5~114℃ Elemental analysis for $C_{13}H_{17}FN_2O_2$ Calcd. % : C,61.89;H,6.79;N,11.10 Found % : C,61.72;H,6.55;N,11.14

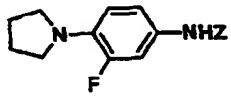
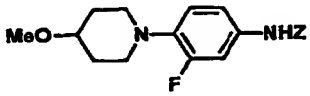
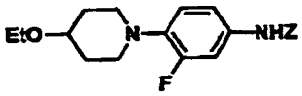
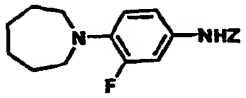
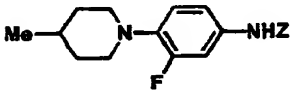
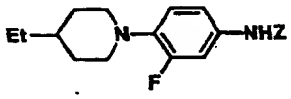
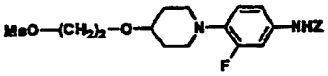
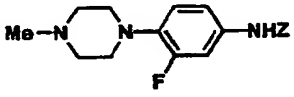
Reference example 37

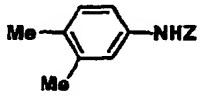
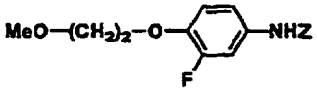
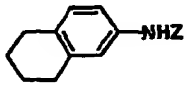
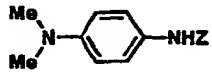
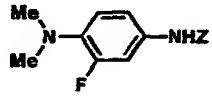
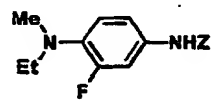
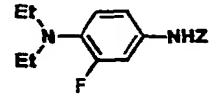
[0067] N-Benzyloxycarbonyl-4-(thiomorpholin-4-yl)aniline

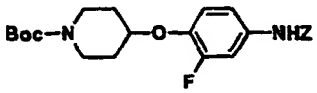
[0068] To a mixture of a solution of 19.0 g of 4-(thiomorpholin-4-yl)aniline in 190 ml of 10% aqueous sodium carbonate and 190 ml of acetone, 21.0 ml of benzyloxycarbonyl chloride was added dropwise under ice-cooling and with stirring. The resulting mixture was stirred at room temperature for 30 minutes, and then the precipitated crystals were collected by filtration, and washed with diisopropyl ether to obtain 25.5 g of pale brown crystals. Recrystallization from a mixture of ethyl acetate-diisopropyl ether gave colorless needles having the melting point of from 145 to 146.5°C.

Elemental analysis for $C_{18}H_{20}N_2O_2S$						
Calculated %	C,	65.83;	H,	6.14;	N,	8.53
Found %	C,	65.69;	H,	6.12;	N,	8.38

[0069] The compounds of Reference examples 38 through 53 were obtained in the same manner as in Reference example 37.

Reference example		Physical properties [recrystallization solvent]
38		pale purple needles [i-PrOH] mp,120～121℃ Elemental analysis for $C_{18}H_{19}FN_2O_2$ Calcd. % : C,68.77;H,6.09;N,8.91 Found % : C,68.88;H,6.00;N,8.88
39		colorless crystals [AcOEt-i-Pr_2O] mp,107～108℃ Elemental analysis for $C_{20}H_{23}FN_2O_3$ Calcd. % : C,67.02;H,6.47;N,7.82 Found % : C,66.90;H,6.35;N,7.73
40		pale purple crystals [i-PrOH] mp,123.5～125℃ Elemental analysis for $C_{21}H_{25}FN_2O_3$ Calcd. % : C,67.72;H,6.77;N,7.52 Found % : C,67.63;H,6.81;N,7.47
41		pale brown needles [AcOEt-i-Pr_2O] mp,78～78.5℃ Elemental analysis for $C_{20}H_{23}FN_2O_2$ Calcd. % : C,70.15;H,6.77;N,8.18 Found % : C,70.10;H,6.77;N,8.17
42		pale purple needles [AcOEt-i-Pr_2O] mp,124.5～126℃ Elemental analysis for $C_{20}H_{23}FN_2O_2$ Calcd. % : C,70.15;H,6.77;N,8.18 Found % : C,70.11;H,6.83;N,8.12
43		pale purple needles [i-PrOH] mp,114～115℃ Elemental analysis for $C_{21}H_{25}FN_2O_2$ Calcd. % : C,70.76;H,7.07;N,7.86 Found % : C,70.66;H,7.17;N,7.84
44		pale brown crystals [AcOEt-i-Pr_2O] mp,97～98.5℃ Elemental analysis for $C_{22}H_{27}FN_2O_4$ Calcd. % : C,65.66;H,6.76;N,6.96 Found % : C,65.59;H,6.98;N,6.96
45		colorless needles [i-PrOH] mp,136.5～137℃ Elemental analysis for $C_{19}H_{22}FN_3O_2$ Calcd. % : C,66.46;H,6.46;N,12.24 Found % : C,66.50;H,6.49;N,12.14

Reference example		Physical properties [recrystallization solvent]
46		colorless crystals [i-Pr_2O] mp,77.5～78℃ Elemental analysis for $C_{16}H_{17}NO_2$ Calcd. % : C,75.27;H,6.71;N,5.49 Found % : C,75.16;H,6.63;N,5.51
47		colorless crystals [AcOEt] mp,91～92℃ Elemental analysis for $C_{17}H_{18}FNO_4$ Calcd. % : C,63.94;H,5.68;N,4.39 Found % : C,63.71;H,5.59;N,4.35
48		colorless needles [i-PrOH] mp,100～100.5℃ Elemental analysis for $C_{18}H_{19}NO_2$ Calcd. % : C,76.84;H,6.81;N,4.98 Found % : C,76.85;H,7.07;N,4.98
49		colorless crystals [AcOEt-i-Pr_2O] mp,106.5～107.5℃ Elemental analysis for $C_{16}H_{18}N_2O_2$ Calcd. % : C,71.09;H,6.71;N,10.36 Found % : C,71.15;H,6.89;N,10.35
50		gray crystals NMR(DMSO-d_6) δ ppm:3.64(6H,s),5.03(2H,s),7.13(2H,d,J=7.5Hz),7.26(1H,dd,J=9,2.5Hz),7.30-7.55(4H,m),7.70-7.75(1H,m),10.3(1H,br-s) IR ν (KBr) cm^{-1}:1740 MS(m/z):288(M^+)
51		colorless crystals [AcOEt-n-Heptane] mp,60～61℃ Elemental analysis for $C_{17}H_{19}FN_2O_2$ Calcd. % : C,67.53;H,6.33;N,9.27 Found % : C,67.32;H,6.33;N,9.29
52		brackish brown liquid NMR(DMSO-d_6) δ ppm:0.96(6H,t,J=7.5Hz),3.06(4H,q,J=7.5Hz),5.15(2H,s),6.95(1H,t,J=9Hz),7.12(1H,dd,J=9,2Hz),7.25-7.45(6H,m),9.62(1H,br-s) IR ν (liq.) cm^{-1}:1706 MS(m/z):316(M^+)

Reference example		Physical properties [recrystallization solvent]
53		reddish brown liquid NMR(DMSO-d6) δ ppm:1.40(9H,s),1.49-1.57(2H,m),1.82-1.88(2H,m),3.13-3.20(2H,m),3.60-3.66(2H,m),4.35-4.41(1H,m),5.14(2H,s),7.10-7.16(2H,m),7.30-7.44(6H,m),9.68(1H,br-s) IR ν (liq.) cm^{-1}:1668,3304 MS(m/z):444(M^+)

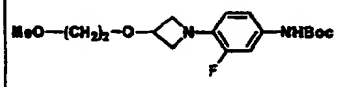
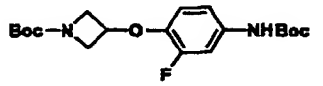
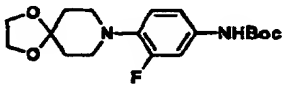
Reference example 54

[0070] N,N'-Di-tert-butoxycarbonyl-3-fluoro-4-(piperazin-1-yl)aniline

[0071] To a solution of 5.56 g of di-tert-butyl dicarbonate in 10 ml of methanol, a solution of 2.00 g of 3-fluoro-4-(piperazin-1-yl)aniline in 10 ml of methanol was added dropwise under stirring at room temperature, and the mixture was stirred overnight at room temperature. The precipitated crystals were collected by filtration, and washed with ethanol to obtain 3.12 g of yellow crystals. Recrystallization from ethyl acetate gave pale yellow crystals having the melting point of from 194 to 195°C.

Elemental analysis for $C_{20}H_{30}FN_3O_4$						
Calculated %	C,	60.74;	H,	7.65;	N,	10.63
Found %	C,	60.47;	H,	7.93;	N,	10.53

[0072] The compounds of Reference examples 55 through 57 were obtained in the same manner as in Referenc example 54.

Reference example		Physical properties [recrystallization solvent]
55		brown liquid NMR(DMSO-d_6) δ ppm:1.45(9H,s),3.26(3H,s),3.44(2H,t,J=4.5Hz),3.52(2H,t,J=4.5Hz),3.55-3.60(2H,m),4.00-4.10(2H,m),4.35-4.40(1H,m),6.46(1H,t,J=8.5Hz),7.04(1H,dd,J=8.5,2Hz),7.22(1H,dd,J=15,2Hz),9.03(1H,br-s) IR ν (liq.) cm^{-1}:1724,3328 MS(m/z):340(M^+)
56		pale brown scales [CH_3CN] mp,220~221℃ Elemental analysis for $C_{19}H_{27}FN_2O_5$ Calcd. % : C,59.67;H,7.12;N,7.33 Found % : C,59.45;H,7.24;N,7.37
57		reddish brown prisms [i-PrOH] mp,139~140.5℃ Elemental analysis for $C_{18}H_{25}FN_2O_4$ Calcd. % : C,61.35;H,7.15;N,7.95 Found % : C,61.30;H,7.37;N,7.98

Reference example 58

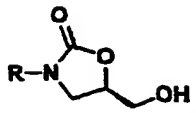
[0073] (R)-5-Hydroxymethyl-2-oxo-3-[4-(thiomorpholin-4-yl)phenyl]oxazolidine

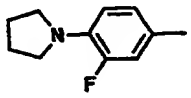
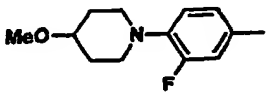
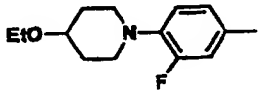
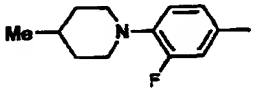
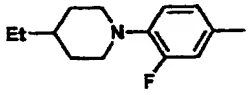
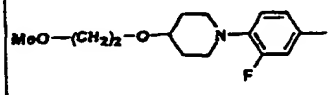
[0074] To a solution of 25.0 g of N-benzyloxycarbonyl-4-(thiomorpholin-4-yl)aniline in 250 ml of dried tetrahydrofuran, 50 ml of 1.63 mol/L n-butyl lithium n-hexane solution was added dropwise with stirring at -78°C under nitrogen flow. Then, the mixture was stirred at the same temperature for 1 hour, added dropwise with 11.5 ml of (R)-(-)-glycidyl butyrate, and stirred at the same temperature for 1 hour, and then at room temperature for 23 hours. The reaction mixture was added with 250 ml of 10% aqueous ammonium chloride, and extracted with ethyl acetate. The extract was washed successively with water and saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was washed with diisopropyl ether to obtain 18.8 g of grayish brown crystals. Recrystallization from ethyl acetate gave colorless crystals having the melting point of from 126.5 to 127.5°C.

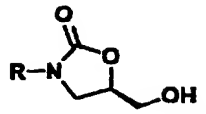
Elemental analysis for $C_{14}H_{18}N_2O_3S$						
Calculated %	C,	57.12;	H,	6.16;	N,	9.52
Found %	C,	56.85;	H,	6.13;	N,	9.25

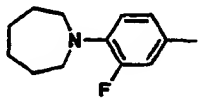
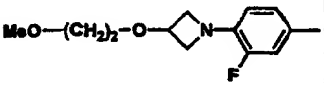
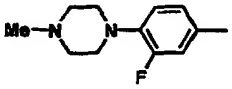
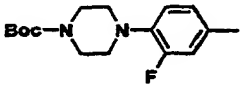
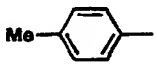
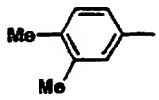
Specific rotation $[\alpha]_D^{20}$ -40.9° (c = 0.1, DMSO)

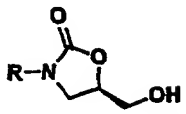
[0075] The compounds of Reference examples 59 through 79 were obtained in the same manner as in Reference example 58.

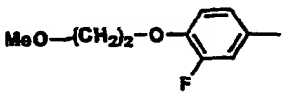
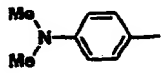
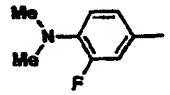
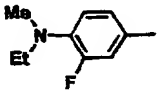
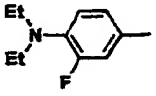


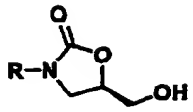
Reference example	R	Physical properties [recrystallization solvent]
59		pale purple needles[EtOH] mp,178~179℃ Elemental analysis for $C_{14}H_{17}FN_2O_3$ Calcd. % : C,59.99;H,6.11;N,9.99 Found % : C,59.97;H,6.06;N,9.98 Specific rotation $[\alpha]_D^{20}$-54.9° (c=0.1,DMSO)
60		pale brown crystals[AcOEt] mp,139.5~141℃ Elemental analysis for $C_{16}H_{21}FN_2O_4$ Calcd. % : C,59.25;H,6.53;N,8.64 Found % : C,58.95;H,6.46;N,8.39 Specific rotation $[\alpha]_D^{20}$-43.1° (c=0.1,DMSO)
61		colorless crystals[i-PrOH] mp,131~132℃ Elemental analysis for $C_{17}H_{23}FN_2O_4$ Calcd. % : C,60.34;H,6.85;N,8.28 Found % : C,60.20;H,7.07;N,8.11 Specific rotation $[\alpha]_D^{20}$-37.0° (c=0.1,DMSO)
62		pale purple needles[AcOEt-i-Pr_2O] mp,141.5~143℃ Elemental analysis for $C_{16}H_{21}FN_2O_3$ Calcd. % : C,62.32;H,6.86;N,9.09 Found % : C,62.21;H,6.94;N,9.01 Specific rotation $[\alpha]_D^{20}$-42.9° (c=0.1,DMSO)
63		colorless needles[i-PrOH] mp,149~149.5℃ Elemental analysis for $C_{17}H_{23}FN_2O_3$ Calcd. % : C,63.34;H,7.19;N,8.69 Found % : C,63.17;H,7.35;N,8.67 Specific rotation $[\alpha]_D^{20}$-43.0° (c=0.1,DMSO)
64		colorless crystals[AcOEt] mp,94.5~96℃ Elemental analysis for $C_{18}H_{25}FN_2O_5$ Calcd. % : C,58.68;H,6.84;N,7.60 Found % : C,58.41;H,7.11;N,7.56 Specific rotation $[\alpha]_D^{20}$-37.9° (c=0.1,DMSO)

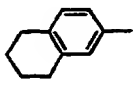
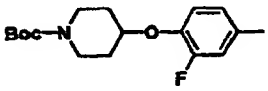
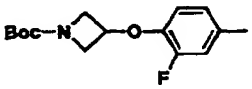
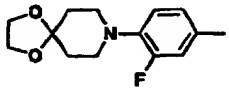


Reference example	R	Physical properties [recrystallization solvent]
65		pale brown prisms [AcOEt-i-Pr$_2$O] mp,118~119℃ Elemental analysis for $C_{16}H_{21}FN_2O_3$ Calcd. % : C,62.32;H,6.86;N,9.09 Found % : C,62.13;H,6.98;N,9.07 Specific rotation $[\alpha]_D^{20}$-36.9° (c=0.1,DMSO)
66		colorless needles [AcOEt] mp,113~114℃ Elemental analysis for $C_{16}H_{21}FN_2O_5$ Calcd. % : C,56.46;H,6.22;N,8.23 Found % : C,56.30;H,6.33;N,8.24 Specific rotation $[\alpha]_D^{20}$-41.2° (c=0.1,DMSO)
67		colorless prisms [i-PrOH] mp,150~151℃ Elemental analysis for $C_{15}H_{20}FN_3O_3$ Calcd. % : C,58.24;H,6.52;N,13.58 Found % : C,58.33;H,6.31;N,13.56 Specific rotation $[\alpha]_D^{20}$-38.9° (c=0.1,DMSO)
68		pale brown prisms [i-PrOH] mp,130~132℃ Elemental analysis for $C_{19}H_{26}FN_3O_5$ Calcd. % : C,57.71;H,6.63;N,10.63 Found % : C,57.55;H,6.87;N,10.57 Specific rotation $[\alpha]_D^{20}$-36.0° (c=0.1,DMSO)
69		pale yellow crystals [EtOH] mp,127.5~128.5℃ Elemental analysis for $C_{11}H_{13}NO_3$ Calcd. % : C,63.76;H,6.32;N,6.76 Found % : C,63.59;H,6.39;N,6.78 Specific rotation $[\alpha]_D^{20}$-55.0° (c=0.1,DMSO)
70		colorless prisms [EtOH] mp,150~151℃ Elemental analysis for $C_{12}H_{15}NO_3$ Calcd. % : C,65.14;H,6.83;N,6.33 Found % : C,65.01;H,6.64;N,6.28 Specific rotation $[\alpha]_D^{20}$-45.9° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
71		pale brown needles[i-PrOH] mp,119～120℃ Elemental analysis for $C_{13}H_{16}FNO_5$ Calcd. % : C,54.73;H,5.65;N,4.91 Found % : C,54.58;H,5.55;N,4.89 Specific rotation $[\alpha]_D^{20}$-40.9° (c=0.1,DMSO)
72		colorless needles[CH_3CN] mp,183～185℃ Elemental analysis for $C_{12}H_{16}N_2O_3$ Calcd. % : C,61.00;H,6.83;N,11.86 Found % : C,60.90;H,6.95;N,11.86 Specific rotation $[\alpha]_D^{20}$-53.8° (c=0.1,DMSO)
73		colorless prisms[AcOEt] mp,128～130℃ Elemental analysis for $C_{12}H_{15}FN_2O_3$ Calcd. % : C,56.69;H,5.95;N,11.02 Found % : C,56.66;H,6.24;N,10.97 Specific rotation $[\alpha]_D^{20}$-51.1° (c=0.1,DMSO)
74		colorless needles[AcOEt-i-Pr_2O] mp,95～96℃ Elemental analysis for $C_{13}H_{17}FN_2O_3$ Calcd. % : C,58.20;H,6.39;N,10.44 Found % : C,58.06;H,6.53;N,10.36 Specific rotation $[\alpha]_D^{20}$-54.8° (c=0.1,DMSO)
75		brown liquid *NMR(DMSO-d6)* δ ppm:0.99(3H,t,J=7.5Hz),3.11(2H,q,J=7.5Hz),3.56(1H,dd,J=12,3.5Hz),3.66(1H,dd,J=12,3.5Hz),3.79(1H,dd,J=9,6.5Hz),4.04(1H,t,J=9Hz),4.60-4.70(1H,m),5.09(1H,br-s),7.03(1H,t,J=9Hz),7.17(1H,dd,J=9,2.5Hz),7.44(1H,dd,J=15,2.5Hz) IR ν (liq.) cm^{-1}:1748,3416 MS(m/z):282(M^+) Specific rotation $[\alpha]_D^{20}$-39.2° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
76		colorless prisms[AcOEt] mp,145.5～146.5℃ Elemental analysis for $C_{14}H_{17}NO_3$ Calcd. % : C,68.00;H,6.93;N,5.66 Found % : C,67.88;H,7.23;N,5.68 Specific rotation $[\alpha]_D^{20}$-51.1° (c=0.1,DMSO)
77		colorless crystals[EtOH] mp,109～110℃ Elemental analysis for $C_{20}H_{27}FN_2O_6$ Calcd. % : C,58.53;H,6.63;N,6.83 Found % : C,58.28;H,6.54;N,6.83 Specific rotation $[\alpha]_D^{20}$-32.0° (c=0.1,DMSO)
78		pale yellowish brown prisms[AcOEt] mp,157～158℃ Elemental analysis for $C_{18}H_{23}FN_2O_6$ Calcd. % : C,56.54;H,6.06;N,7.33 Found % : C,56.42;H,6.32;N,7.26 Specific rotation $[\alpha]_D^{20}$-30.1° (c=0.1,DMSO)
79		pale purple prisms[i-PrOH] mp,163～165.5℃ Elemental analysis for $C_{17}H_{21}FN_2O_5$ Calcd. % : C,57.95;H,6.01;N,7.95 Found % : C,57.89;H,6.04;N,7.92 Specific rotation $[\alpha]_D^{20}$-41.1° (c=0.1,DMSO)

Reference example 80

[0076] (R)-5-Mesyloxymethyl-2-oxo-3-[4-(thiomorpholin-4-yl)phenyl]oxazolidine

[0077] To a solution of 10.0 g of (R)-5-hydroxymethyl-2-oxo-3-[4-(thiomorpholin-4-yl)phenyl]oxazolidine and 10.5 ml of triethylamine in 200 ml of dichloromethane, 3.20 ml of methanesulfonyl chloride was added dropwise under ice-cooling and with stirring, and then the mixture was stirred at room temperature for 2 hours. The reaction solution was added with 200 ml of water, and extracted with dichloromethane. The extract was washed successively with water and saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was washed with diisopropyl ether to obtain 11.5 g of grayish brown crystals. Recrystallization from ethyl acetate gave colorless prisms having the melting point of from 174.5 to 175.5°C.

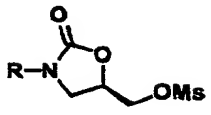
Elemental analysis for $C_{15}H_{20}N_2O_5S_2$						
Calculated %	C,	48.37;	H,	5.41;	N,	7.52

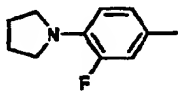
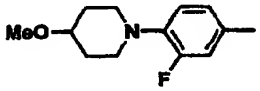
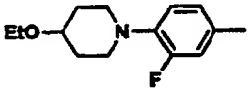
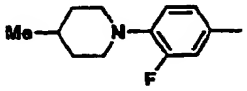
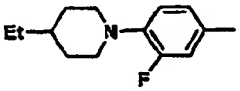
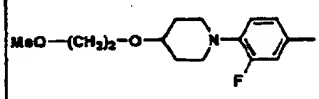
(continued)

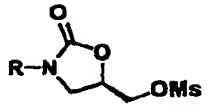
Elemental analysis for $C_{15}H_{20}N_2O_5S_2$						
Found %	C,	48.41;	H,	5.33;	N,	7.36

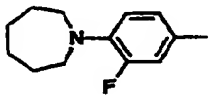
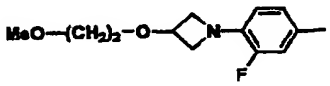
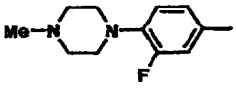
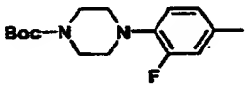
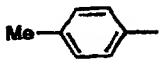
Specific rotation $[\alpha]_D^{20}$ -54.2° (c = 0.1, DMSO)

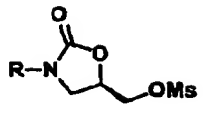
[0078] The compounds of Reference examples 81 through 101 were obtained in the same manner as in Reference example 80.

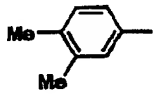
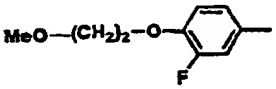
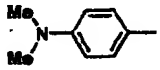
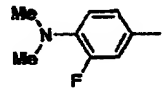
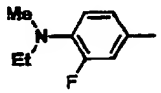


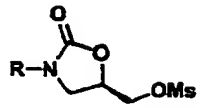
Reference example	R	Physical properties [recrystallization solvent]
81		colorless crystals[AcOEt-i-Pr$_2$O] mp,111～112℃ Elemental analysis for $C_{15}H_{19}FN_2O_5S$ Calcd. % : C,50.27;H,5.34;N,7.82 Found % : C,50.10;H,5.30;N,7.73 Specific rotation [α]$_D^{20}$-50.1° (c=0.1,DMSO)
82		colorless prisms[AcOEt] mp,124.5～125.5℃ Elemental analysis for $C_{17}H_{23}FN_2O_6S$ Calcd. % : C,50.74;H,5.76;N,6.96 Found % : C,50.50;H,5.66;N,6.87 Specific rotation [α]$_D^{20}$-49.9° (c=0.1,DMSO)
83		colorless needles[i-PrOH] mp,128～128.5℃ Elemental analysis for $C_{18}H_{25}FN_2O_6S$ Calcd. % : C,51.91;H,6.05;N,6.73 Found % : C,51.80;H,6.29;N,6.69 Specific rotation [α]$_D^{20}$-47.9° (c=0.1,DMSO)
84		pale purple prisms[i-PrOH] mp,155～156.5℃ Elemental analysis for $C_{17}H_{23}FN_2O_5S$ Calcd. % : C,52.84;H,6.00;N,7.25 Found % : C,52.65;H,6.22;N,7.07 Specific rotation [α]$_D^{20}$-52.9° (c=0.1,DMSO)
85		colorless plates[EtOH] mp,155～156℃ Elemental analysis for $C_{18}H_{25}FN_2O_5S$ Calcd. % : C,53.99;H,6.29;N,7.00 Found % : C,53.74;H,6.40;N,6.87 Specific rotation [α]$_D^{20}$-51.1° (c=0.1,DMSO)
86		pale brown needles[AcOEt] mp,124～124.5℃ Elemental analysis for $C_{19}H_{27}FN_2O_7S$ Calcd. % : C,51.11;H,6.10;N,6.27 Found % : C,50.82;H,6.34;N,6.25 Specific rotation [α]$_D^{20}$-47.8° (c=0.1,DMSO)

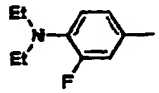
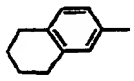
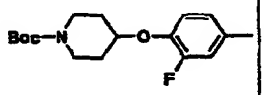
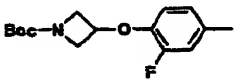
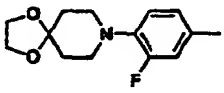


Reference example	R	Physical properties [recrystallization solvent]
87		colorless needles[AcOEt-i-Pr_2O] mp,121～122.5℃ Elemental analysis for $C_{17}H_{23}FN_2O_5S$ Calcd. % : C,52.84;H,6.00;N,7.25 Found % : C,52.57;H,6.16;N,7.20 Specific rotation $[\alpha]_D^{20}$-52.8° (c=0.1,DMSO)
88		brown liquid NMR(DMSO-d_6) δ ppm:3.22(3H,s),3.26(3H,s),3.45(2H,t,J=5Hz),3.53(2H,t,J=5Hz),3.60-3.70(2H,m),3.77(1H,dd,J=9.5,6.5Hz),4.10-4.15(3H,m),4.35-4.45(1H,m),4.44(1H,dd,J=11.5,5.5Hz),4.49(1H,dd,J=11.5,3Hz),4.90-5.00(1H,m),6.58(1H,t,J=9Hz),7.12(1H,dd,J=9,2.5Hz),7.37(1H,dd,J=14.5,2.5Hz) IR ν (liq.) cm^{-1}:1754 MS(m/z):418(M^+) Specific rotation $[\alpha]_D^{20}$-45.7° (c=0.1,DMSO)
89		colorless prisms[AcOEt] mp,159.5～160.5℃ Elemental analysis for $C_{16}H_{22}FN_3O_5S$ Calcd. % : C,49.60;H,5.72;N,10.85 Found % : C,49.58;H,5.46;N,10.75 Specific rotation $[\alpha]_D^{20}$-49.0° (c=0.1,DMSO)
90		colorless prisms[MeOH] mp,182.5～183.5℃ Elemental analysis for $C_{20}H_{28}FN_3O_7S$ Calcd. % : C,50.73;H,5.96;N,8.87 Found % : C,50.63;H,6.11;N,8.88 Specific rotation $[\alpha]_D^{20}$-46.0° (c=0.1,DMSO)
91		pale brown crystals[i-PrOH] mp,128～130℃ Elemental analysis for $C_{12}H_{15}NO_5S$ Calcd. % : C,50.52;H,5.30;N,4.91 Found % : C,50.23;H,5.30;N,4.83 Specific rotation $[\alpha]_D^{20}$-54.0° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
92		pale yellow prisms [i-PrOH] mp,113~113.5℃ Elemental analysis for $C_{13}H_{17}NO_5S$ Calcd. % : C,52.16;H,5.72;N,4.68 Found % : C,51.91;H,5.56;N,4.63 Specific rotation $[\alpha]_D^{20}$-52.9° (c=0.1,DMSO)
93		colorless crystals [EtOH] mp,72.5~74℃ Elemental analysis for $C_{14}H_{18}FNO_7S$ Calcd. % : C,46.28;H,4.99;N,3.85 Found % : C,46.22;H,4.95;N,3.83 Specific rotation $[\alpha]_D^{20}$-51.2° (c=0.1,DMSO)
94		colorless prisms [AcOEt-i-Pr_2O] mp,141.5~143℃ Elemental analysis for $C_{13}H_{18}N_2O_5S$ Calcd. % : C,49.67;H,5.77;N,8.91 Found % : C,49.41;H,5.64;N,8.84 Specific rotation $[\alpha]_D^{20}$-55.9° (c=0.1,DMSO)
95		pale yellowish brown amorphous solid NMR(DMSO-d_6) δ ppm:2.88(6H,s),3.23(3H,s),3.82(1H,dd,J=9,6Hz),4.18(1H,t,J=9Hz),4.45(1H,dd,J=11.5,5.5Hz),4.50(1H,dd,J=11.5,3Hz),4.95-5.05(1H,m),7.20-7.30(2H,m),7.52(1H,d,J=14Hz) IR ν (liq.) cm^{-1}:1758 MS(m/z):332(M^+) Specific rotation $[\alpha]_D^{20}$-41.5° (c=0.1,DMSO)
96		pale purple crystals [AcOEt-i-Pr_2O] mp,66~67℃ Elemental analysis for $C_{14}H_{19}FN_2O_5S$ Calcd. % : C,48.55;H,5.53;N,8.09 Found % : C,48.20;H,5.64;N,7.94 Specific rotation $[\alpha]_D^{20}$-58.5° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
97		brown liquid NMR(DMSO-d_6) δ ppm:1.00(6H,t,J=7Hz),3.15(4H,q,J=7Hz),3.23(3H,s),3.81(1H,dd,J=9,6Hz),4.16(1H,t,J=9Hz),4.45(1H,dd,J=11.5,5.5Hz),4.50(1H,dd,J=11.5,3Hz),4.95-5.05(1H,m),7.05-7.15(1H,m),7.15-7.25(1H,m),7.40-7.50(1H,m) IR ν (liq.) cm^{-1}:1178,1360,1756 MS(m/z):360(M^+) Specific rotation [α]$_D^{20}$-42.2° (c=0.1,DMSO)
98		colorless needles[i-PrOH] mp,100.5~102.5℃ Elemental analysis for $C_{16}H_{19}NO_5S$ Calcd. % : C,55.37;H,5.89;N,4.30 Found % : C,55.11;H,6.02;N,4.27 Specific rotation [α]$_D^{20}$-58.1° (c=0.1,DMSO)
99		colorless prisms[i-PrOH] mp,126~127.5℃ Elemental analysis for $C_{21}H_{29}FN_2O_8S$ Calcd. % : C,51.63;H,5.98;N,5.73 Found % : C,51.44;H,6.18;N,5.68 Specific rotation [α]$_D^{20}$-37.9° (c=0.1,DMSO)
100		colorless prisms[i-PrOH] mp,114.5~117℃ Elemental analysis for $C_{19}H_{25}FN_2O_8S$ Calcd. % : C,49.56;H,5.47;N,6.08 Found % : C,49.46;H,5.67;N,6.03 Specific rotation [α]$_D^{20}$-46.0° (c=0.1,DMSO)
101		pale purple scales[AcOEt] mp,147.5~149℃ Elemental analysis for $C_{18}H_{23}FN_2O_7S$ Calcd. % : C,50.22;H,5.39;N,6.51 Found % : C,50.06;H,5.66;N,6.49 Specific rotation [α]$_D^{20}$-45.8° (c=0.1,DMSO)

Reference example 102

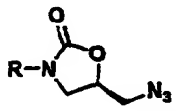
[0079] (R)-5-Azidomethyl-2-oxo-3-[4-(thiomorpholin-4-yl)phenyl]oxazolidine

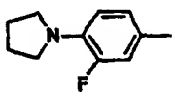
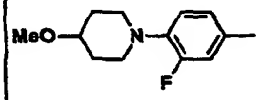
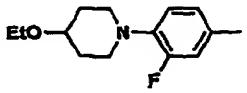
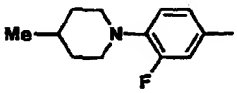
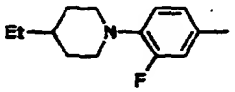
[0080] A suspension of 11.5 g of (R)-5-mesyloxymethyl-2-oxo-3-[4-(thiomorpholin-4-yl)phenyl]oxazolidine and 8.35 g of sodium azide in 110 ml of dried N,N-dimethylformamide was stirred with heating to 65°C for 5 hours. The reaction solution was cooled, then added with 200 ml of water, and extracted with ethyl acetate. The extract was washed successively with water and saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was washed with diisopropyl ether to obtain 8.85 g of grayish brown crystals. Recrystallization from ethyl acetate gave colorless crystals having the melting point of from 110 to 111°C.

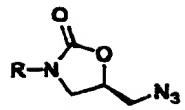
Elemental analysis for $C_{14}H_{17}N_5O_2S$						
Calculated %	C,	52.65;	H,	5.37;	N,	21.93
Found %	C,	52.47;	H,	5.35;	N,	21.65

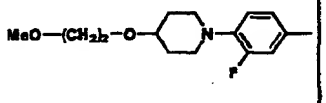
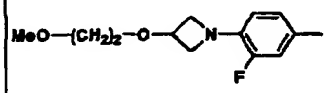
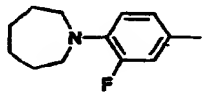
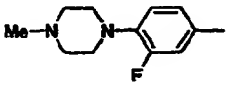
Specific rotation $[\alpha]_D^{20}$ -124.4° (c = 0.1, DMSO)

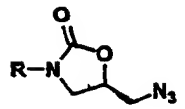
[0081] The compounds of Reference examples 103 through 123 were obtained in the same manner as in Reference example 102.

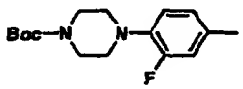
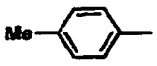
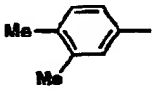
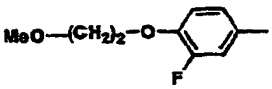
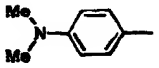


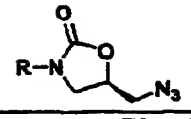
Reference example	R	Physical properties [recrystallization solvent]
103		colorless crystals[AcOEt] mp,109~109.5℃ Elemental analysis for $C_{14}H_{16}FN_5O_2$ Calcd. % : C,55.08;H,5.28;N,22.94 Found % : C,54.88;H,5.12;N,22.70 Specific rotation $[\alpha]_D^{20}$-136.4° (c=0.1,DMSO)
104		colorless needles[AcOEt-i-Pr_2O] mp,89~90℃ Elemental analysis for $C_{16}H_{20}FN_5O_3$ Calcd. % : C,55.01;H,5.77;N,20.05 Found % : C,54.83;H,5.72;N,19.88 Specific rotation $[\alpha]_D^{20}$-118.5° (c=0.1,DMSO)
105		pale brown needles[i-PrOH] mp,66~67℃ Elemental analysis for $C_{17}H_{22}FN_5O_3$ Calcd. % : C,56.19;H,6.10;N,19.27 Found % : C,56.05;H,6.36;N,19.23 Specific rotation $[\alpha]_D^{20}$-110.5° (c=0.1,DMSO)
106		pale purple prisms[AcOEt-i-Pr_2O] mp,97.5~98.5℃ Elemental analysis for $C_{16}H_{20}FN_5O_2$ Calcd. % : C,57.65;H,6.05;N,21.01 Found % : C,57.69;H,6.21;N,20.90 Specific rotation $[\alpha]_D^{20}$-122.4° (c=0.1,DMSO)
107		colorless plates[EtOH] mp,99~100℃ Elemental analysis for $C_{17}H_{22}FN_5O_2$ Calcd. % : C,58.78;H,6.38;N,20.16 Found % : C,58.66;H,6.47;N,20.06 Specific rotation $[\alpha]_D^{20}$-117.3° (c=0.1,DMSO)

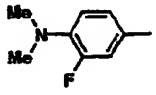
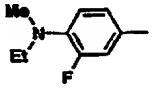
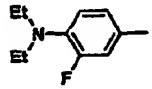
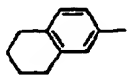


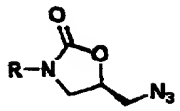
Reference example	R	Physical properties [recrystallization solvent]
108		pale brown liquid NMR(DMSO-d_6) δ ppm:1.55-1.65(2H,m),1.90-2.00(2H,m),2.75-2.80(2H,m),3.15-3.25(2H,m),3.27(3H,s),3.40-3.50(1H,m),3.45(2H,t,J=5Hz),3.56(2H,t,J=5Hz),3.67(1H,dd,J=13.5,6Hz),3.70-3.80(2H,m),4.10(1H,t,J=9Hz),4.80-4.90(1H,m),7.06(1H,t,J=9Hz),7.17(1H,dd,J=9,2.5Hz),7.45(1H,dd,J=15,2.5Hz) IR ν (liq.) cm^{-1}:1756,2112 MS(m/z):393(M^+) Specific rotation $[\alpha]_D^{20}$-100.3° (c=0.1,DMSO)
109		brown liquid NMR(DMSO-d_6) δ ppm:3.26(3H,s),3.45(2H,t,J=4.5Hz),3.53(2H,t,J=4.5Hz),3.60-3.75(5H,m),4.08(1H,t,J=9Hz),4.05-4.15(2H,m),4.35-4.45(1H,m),4.80-4.90(1H,m),6.58(1H,t,J=8.5Hz),7.12(1H,dd,J=8.5,2Hz),7.38(1H,dd,J=14.5,2Hz) IR ν (liq.) cm^{-1}:1752,2112 MS(m/z):365(M^+) Specific rotation $[\alpha]_D^{20}$-91.4° (c=0.1,DMSO)
110		colorless crystals[AcOEt-i-Pr_2O] mp,67～67.5℃ Elemental analysis for $C_{16}H_{20}FN_5O_2$ Calcd. % : C,57.65;H,6.05;N,21.01 Found % : C,57.66;H,6.09;N,21.05 Specific rotation $[\alpha]_D^{20}$-122.6° (c=0.1,DMSO)
111		colorless scales[i-PrOH] mp,106.5～107℃ Elemental analysis for $C_{15}H_{19}FN_6O_2$ Calcd. % : C,53.88;H,5.73;N,25.14 Found % : C,53.88;H,5.63;N,25.14 Specific rotation $[\alpha]_D^{20}$-118.5° (c=0.1,DMSO)

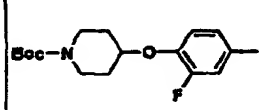
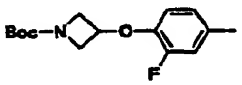
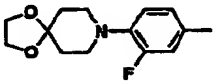


Reference example	R	Physical properties [recrystallization solvent]
112		pale brown needles[i-PrOH] mp,112～113℃ Elemental analysis for $C_{19}H_{25}FN_6O_4$ Calcd. % : C,54.28;H,5.99;N,19.99 Found % : C,54.20;H,6.09;N,20.07 Specific rotation [α]$_D^{20}$-101.9° (c=0.1,DMSO)
113		reddish brown liquid NMR($CDCl_3$) δ ppm:2.33(3H,s),3.59(1H,dd,J=13.5,4.5Hz),3.68(1H,dd,J=13.5,4.5Hz),3.84(1H,dd,J=9,6Hz),4.08(1H,t,J=9Hz),4.74-4.80(1H,m),7.18(2H,d,J=8Hz),7.41(2H,d,J=8Hz) IR ν (liq.) cm^{-1}:1754,2112 MS(m/z):232(M^+) Specific rotation [α]$_D^{20}$-119.1° (c=0.1,DMSO)
114		pale brown crystals[i-Pr_2O] mp,85～85.5℃ Elemental analysis for $C_{13}H_{14}N_4O_2$ Calcd. % : C,58.53;H,5.73;N,22.75 Found % : C,58.30;H,5.59;N,22.46 Specific rotation [α]$_D^{20}$-140.4° (c=0.1,DMSO)
115		colorless plates[EtOH] mp,75～76℃ Elemental analysis for $C_{13}H_{15}FN_4O_4$ Calcd. % : C,50.32;H,4.87;N,18.06 Found % : C,50.27;H,4.94;N,18.01 Specific rotation [α]$_D^{20}$-119.8° (c=0.1,DMSO)
116		colorless prisms[AcOEt] mp,112～113℃ Elemental analysis for $C_{12}H_{15}N_5O_2$ Calcd. % : C,55.16;H,5.79;N,26.80 Found % : C,55.12;H,5.60;N,26.73 Specific rotation [α]$_D^{20}$-142.0° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
117		pale brown crystals NMR(DMSO-d_6) δ ppm:2.75(6H,s),3.66(1H,dd,J=13.5,5.5Hz),3.70-3.75(2H,m),4.10(1H,t,J=9Hz),4.80-4.90(1H,m),6.98(1H,t,J=9Hz),7.15(1H,dd,J=9,2.5Hz),7.43(1H,dd,J=15,2.5Hz) IR ν (KBr) cm^{-1}:1752,2108 MS(m/z):279(M^+) Specific rotation [α]$_D^{20}$-137.8° (c=0.1,DMSO)
118		brown liquid NMR(DMSO-d_6) δ ppm:1.03(3H,t,J=7Hz),2.73(3H,s),3.12(2H,q,J=7Hz),3.67(1H,dd,J=13.5,5.5Hz),3.70-3.80(2H,m),4.10(1H,t,J=9Hz),4.80-4.90(1H,m),6.98(1H,t,J=9Hz),7.16(1H,dd,J=9,2.5Hz),7.42(1H,dd,J=15.5,2.5Hz) IR ν (liq.) cm^{-1}:1756,2112 MS(m/z):293(M^+) Specific rotation [α]$_D^{20}$-134.8° (c=0.1,DMSO)
119		brown liquid NMR(DMSO-d_6) δ ppm:0.99(6H,t,J=7.5Hz),3.12(4H,q,J=7.5Hz),3.67(1H,dd,J=13.5,5.5Hz),3.70-3.80(2H,m),4.11(1H,t,J=9Hz),4.80-4.90(1H,m),7.03(1H,t,J=9Hz),7.17(1H,dd,J=9,2.5Hz),7.42(1H,dd,J=15.5,2.5Hz) IR ν (liq.) cm^{-1}:1756,2112 MS(m/z):307(M^+) Specific rotation [α]$_D^{20}$-105.8° (c=0.1,DMSO)
120		colorless needles[i-PrOH] mp,104～105.5℃ Elemental analysis for $C_{14}H_{16}N_4O_2$ Calcd. % : C,61.75;H,5.92;N,20.58 Found % : C,61.64;H,5.73;N,20.54 Specific rotation [α]$_D^{20}$-135.9° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
121		colorless prisms [i-PrOH] mp,111~112.5℃ Elemental analysis for $C_{20}H_{26}FN_5O_5$ Calcd. % : C,55.16;H,6.02;N,16.08 Found % : C,55.07;H,6.15;N,15.88 Specific rotation $[\alpha]_D^{20}$-86.3° (c=0.1,DMSO)
122		colorless prisms [i-PrOH] mp,122~123℃ Elemental analysis for $C_{18}H_{22}FN_5O_5$ Calcd. % : C,53.07;H,5.44;N,17.19 Found % : C,53.02;H,5.66;N,17.22 Specific rotation $[\alpha]_D^{20}$-96.8° (c=0.1,DMSO)
123		pale brown prisms [i-PrOH] mp,114.5~116℃ Elemental analysis for $C_{17}H_{20}FN_5O_4$ Calcd. % : C,54.11;H,5.34;N,18.56 Found % : C,54.32;H,5.32;N,18.26 Specific rotation $[\alpha]_D^{20}$-113.0° (c=0.1,DMSO)

Reference example 124

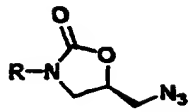
[0082] (R)-5-Azidomethyl-3-[3-fluoro-4-(piperazin-1-yl)phenyl]-2-oxooxazolidine

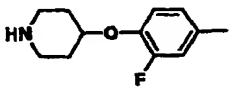
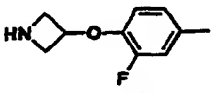
[0083] To 1.00 g of (R)-5-azidomethyl-3-[4-(4-tert-butoxycarbonylpiperazin-1-yl)-3-fluorophenyl]-2-oxooxazolidine, 20 ml of 16 % hydrogen chloride ethyl acetate solution was added, and the mixture was stirred at room temperature for 30 minutes. The precipitated crystals were collected by filtration. The crystals were added with aqueous sodium hydroxide, and then the resulting alkaline mixture was extracted with ethyl acetate. The extract was washed with saturated brine and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure to obtain 0.72 g of pale brown crystals. Recrystallization from isopropanol gave colorless crystals having the melting point of from 114 to 115°C.

Elemental analysis for $C_{14}H_{17}FN_6O_2$						
Calculated %	C,	52.49;	H,	5.35;	N,	26.24
Found %	C,	52.24;	H,	5.21;	N,	26.15

Specific rotation $[\alpha]_D^{20}$ -127.3° (c = 0.1, DMSO)

[0084] The compounds of Reference examples 125 through 126 were obtained in the same manner as in Reference example 124.



Reference example	R	Physical properties [recrystallization solvent]
125	 · HCl	colorless prisms [MeOH] mp,169~170°C Elemental analysis for $C_{15}H_{18}FN_5O_3 \cdot HCl$ Calcd. % : C,48.46;H,5.15;N,18.84 Found % : C,48.23;H,5.12;N,18.65 Specific rotation $[\alpha]_D^{20}$-99.8° (c=0.1,DMSO)
126	 · HCl	pale brown crystals NMR(DMSO-d_6) δ ppm:3.67(1H,dd,J=14,6Hz),3.70-3.80(2H,m),4.02(2H,dd,J=12,5Hz),4.12(1H,t,J=9Hz),4.41(2H,dd,J=12,7Hz),4.80-4.90(1H,m),5.05-5.15(1H,m),7.05(1H,t,J=9Hz),7.22(1H,dd,J=9,2Hz),7.60(1H,dd,J=13.5,2Hz),9.46(1H,br-s) IR ν (KBr) cm^{-1}:1744,2116 Specific rotation $[\alpha]_D^{20}$-108.6° (c=0.1,DMSO)

Reference example 127

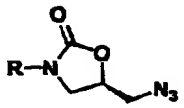
[0085] (R)-5-Azidomethyl-3-[4-(4-ethylpiperazin-1-yl)-3-fluorophenyl]-2-oxo-oxazolidine

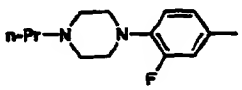
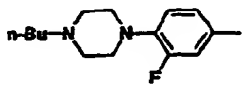
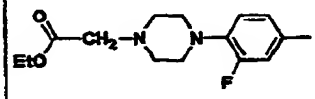
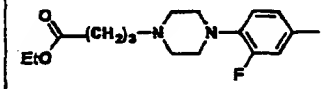
[0086] To a solution of 5.00 g of (R)-5-azidomethyl-3-[3-fluoro-4-(piperazin-1-yl)phenyl]-2-oxooxazolidine and 2.16 g of potassium carbonate in 50 ml of dried N,N-dimethylformamide, 1.40 ml of ethyl iodide was added dropwise at room temperature, and the mixture was stirred at room temperature for 3 hours. The reaction solution was added with water, and extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure to obtain 4.53 g of pale brown crystals. Recrystallization from a mixture of ethyl acetate and n-heptane gave colorless crystals having the melting point of from 90 to 91°C.

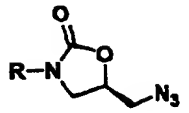
Elemental analysis for $C_{16}H_{21}FN_6O_2$						
Calculated %	C,	55.16;	H,	6.08;	N,	24.12
Found %	C,	55.22;	H,	6.20;	N,	24.03

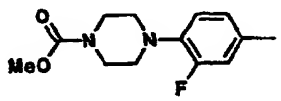
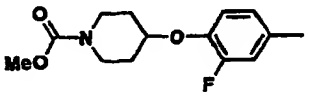
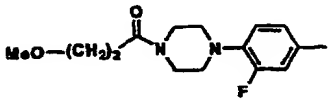
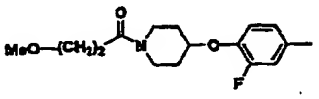
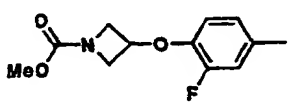
Specific rotation $[\alpha]_D^{20}$ -120.9° (c = 0.1, DMSO)

[0087] The compounds of Reference examples 128 through 136 were obtained in the same manner as in Reference example 127.



Reference example	R	Physical properties [recrystallization solvent]
128		pale brown needles[i-PrOH] mp,113.5～114.5℃ Elemental analysis for $C_{17}H_{23}FN_6O_2$ Calcd. % : C,56.34;H,6.40;N,23.19 Found % : C,56.32;H,6.48;N,23.17 Specific rotation [α]$_D^{20}$-114.3° (c=0.1,DMSO)
129		pale yellow scales[i-PrOH] mp,102～103℃ Elemental analysis for $C_{18}H_{25}FN_6O_2 \cdot 1/8H_2O$ Calcd. % : C,57.09;H,6.72;N,22.19 Found % : C,57.10;H,6.86;N,22.20 Specific rotation [α]$_D^{20}$-104.8° (c=0.1,DMSO)
130		colorless needles[AcOEt-i-Pr$_2$O] mp,125～126.5℃ Elemental analysis for $C_{18}H_{23}FN_6O_4$ Calcd. % : C,53.20;H,5.70;N,20.68 Found % : C,53.03;H,5.47;N,20.49 Specific rotation [α]$_D^{20}$-101.5° (c=0.1,DMSO)
131		colorless crystals[AcOEt-i-Pr$_2$O] mp,64.5～66℃ Elemental analysis for $C_{20}H_{27}FN_6O_4$ Calcd. % : C,55.29;H,6.26;N,19.34 Found % : C,55.25;H,6.33;N,19.31 Specific rotation [α]$_D^{20}$-89.0° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
132		pale brown prisms [EtOH] mp,105~106℃ Elemental analysis for $C_{16}H_{19}FN_6O_4$ Calcd. % : C,50.79;H,5.06;N,22.21 Found % : C,50.66;H,5.16;N,22.20 Specific rotation $[\alpha]_D^{20}$-103.9° (c=0.1,DMSO)
133		pale brown prisms [i-PrOH] mp,80~81.5℃ Elemental analysis for $C_{17}H_{20}FN_5O_5$ Calcd. % : C,51.91;H,5.12;N,17.80 Found % : C,51.91;H,4.87;N,17.75 Specific rotation $[\alpha]_D^{20}$-98.6° (c=0.1,DMSO)
134		pale yellow prisms [EtOH] mp,99~101℃ Elemental analysis for $C_{18}H_{23}FN_6O_4$ Calcd. % : C,53.20;H,5.70;N,20.68 Found % : C,53.07;H,5.68;N,20.75 Specific rotation $[\alpha]_D^{20}$-106.9° (c=0.1,DMSO)
135		pale yellow liquid NMR(DMSO-d_6) δ ppm:1.50-1.70(2H,m),1.80-2.00(2H,m),2.57(2H,t,J=6Hz),3.20-3.40(2H,m),3.23(3H,s),3.56(2H,t,J=6Hz),3.65-3.85(4H,m),3.67(1H,dd,J=13.5,5.5Hz),4.12(1H,t,J=9Hz),4.50-4.60(1H,m),4.80-4.90(1H,m),7.22(1H,dd,J=9,2.5Hz),7.27(1H,t,J=9Hz),7.54(1H,dd,J=13.5,2.5Hz) IR ν (liq.) cm^{-1}:1756,2112 MS(m/z):421(M^+) Specific rotation $[\alpha]_D^{20}$-86.2° (c=0.1,DMSO)
136		pale brown prisms [i-PrOH] mp,82~83℃ Elemental analysis for $C_{15}H_{16}FN_5O_5$ Calcd. % : C,49.32;H,4.41;N,19.17 Found % : C,49.05;H,4.32;N,19.18 Specific rotation $[\alpha]_D^{20}$-103.9° (c=0.1,DMSO)

Reference example 137

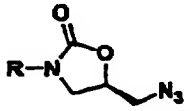
[0088] Ethyl (R)-3-[4-[4-(5-azidomethyl-2-oxooxazolidin-3-yl)-2-fluorophenyl]-piperazin-1-yl]propionate

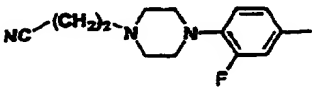
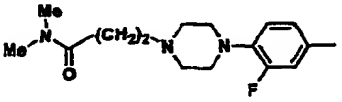
[0089] A solution of 7.00 g of (R)-5-azidomethyl-3-[3-fluoro-4-(piperazin-1-yl)-phenyl]-2-oxooxazolidine and 3.56 ml of ethyl acrylate_ in 70 ml of ethanol was heated under reflux for 1 hour. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (silica gel, diethyl ether) to obtain 7.50 g of colorless crystals. Recrystallization from isopropanol gave colorless crystals having the melting point of from 82 to 83°C.

Elemental analysis for $C_{19}H_{25}FN_6O_4$						
Calculated %	C,	54.28;	H,	5.99;	N,	19.99
Found %	C,	53.99;	H,	5.88;	N,	19.97

Specific rotation $[\alpha]_D^{20}$ -95.0° (c = 0.1, DMSO)

[0090] The compounds of Reference examples 138 through 139 were obtained in the same manner as in Reference example 137.



Reference example	R	Physical properties [recrystallization solvent]
138		pale brown needles [MeOH] mp,110~112°C Elemental analysis for $C_{17}H_{20}FN_7O_2$ Calcd. % : C,54.68;H,5.40;N,26.26 Found % : C,54.65;H,5.39;N,26.04 Specific rotation $[\alpha]_D^{20}$-114.8° (c=0.1,DMSO)
139		colorless needles [AcOEt] mp,130.5~131.5°C Elemental analysis for $C_{19}H_{26}FN_7O_3$ Calcd. % : C,54.40;H,6.25;N,23.38 Found % : C,54.37;H,6.35;N,23.20 Specific rotation $[\alpha]_D^{20}$-100.0° (c=0.1,DMSO)

Reference example 140

[0091] (R)-5-Azidomethyl-3-[3-fluoro-4-[4-(3-phthalimidopropyl)piperazin-1-yl]-phenyl]-2-oxooxazolidine

[0092] To a suspension of 5.00 g of (R)-5-azidomethyl-3-[3-fluoro-4-(piperazin-1-yl)phenyl]-2-oxooxazolidine and 2.16 g of potassium _ carbonate in 110 ml of dried N,N-dimethyformamide, 4.60 g of N-(3-bromopropyl)phthalimide was added, and the mixture was stirred with heating at an outer temperature of 50°C for 3 hours. The reaction solution was added with water, and extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was washed with diisopropyl ether to obtain 6.54 g of pale brown crystals. Recrystallization from ethyl acetate gave colorless needles having the melting point of from 153 to 154.5°C.

Elemental analysis for $C_{25}H_{26}FN_7O_4$						
Calculated %	C,	59.16;	H,	5.16;	N,	19.32
Found %	C,	58.99;	H,	5.02;	N,	19.29

Specific rotation $[\alpha]_D^{20}$ -95.3° (c = 0.1, DMSO)

[0093] The compound of Reference example 141 was obtained in the same manner as in Reference example 140.

Reference example 141

[0094] (R)-5-Azidomethyl-3-[3-fluoro-4-[4-(2-phthalimidoethyl)piperazin-1-yl]-phenyl]-2-oxooxazolidine
Appearance : pale yellow crystals (recrystallization solvent : DMF-H_2O)
Melting point : 210.5 to 212°C

Elemental analysis for $C_{24}H_{24}FN_7O_4$						
Calculated %	C,	58.41;	H,	4.90;	N,	19.87
Found %	C,	58.04;	H,	4.67;	N,	19.72

Specific rotation $[\alpha]_D^{20}$ -95.1° (c = 0.1, DMSO)

Refer nce example 142

[0095] (R)-3-[4-[4-(3-Aminopropyl)piperazin-1-yl]-3-fluorophenyl]-5-azidomethyl-2-oxooxazolidine
[0096] To a solution of 6.24 g of (R)-5-azidomethyl-3-[3-fluoro-4-[4-(3-phthalimidopropyl)piperazin-1-yl]phenyl]-2-oxooxazolidine in 60 ml of ethanol, 0.66 ml of hydrazine hydrate was added, and the mixture was heated under reflux for 4 hours. The reaction solution was added with water, and acidified with 10 % hydrochloric acid, and the aqueous layer was washed with ethyl acetate. The aqueous layer was alkalified with aqueous sodium hydroxide, and extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure to obtain 4.35 g of a pale brown liquid.
NMR spectrum (DMSO-d_6) δ ppm:
1.55(2H,quin,J=7Hz),2,37(2H,t,J=7Hz),2.51(4H,t,J=4.5Hz),2.62(2H,t,J=7Hz), 2.99(4H,t,J=4.5Hz),3.67(1H,dd, J=13.5,5.5Hz),3.70-3.80(2H,m),4.10(1H,t,J=9Hz), 4.80-4.90(1H,m),7.04(1H,t,J=9Hz),7.18(1H,dd,J=9,2.5Hz),7.46 (1H,dd,J=15,2.5Hz)
IR spectrum ν (liq.) cm^{-1}: 1752,2112
Mass spectrum (m/z) : 377(M^+)
Specific rotation $[\alpha]_D^{20}$ -116.9° (c = 0.1, DMSO)

Ref rence example 143

[0097] (R)-3-[4-[4-(3-Acetylaminopropyl)piperazin-1-yl]-3-fluorophenyl]-5-azidomethyl-2-oxooxazolidine
[0098] To a solution of 2.00 g of (R)-3-[4-[4-(3-aminopropyl)piperazin-1-yl]-3-fluorophenyl]-5-azidomethyl-2-oxooxazolidine in 20 ml of pyridine, 1.50 ml of acetic anhydride was added under ice-cooling and with stirring, and the mixture was stirred at the same temperature for 1 hour. The solvent was evaporated under reduced pressure, and then th residue was added with aqueous sodium hydroxide, and the resulting alkaline mixture was extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (alumina, ethyl acetate to ethyl acetate : methanol = 20 : 1) to obtain 1.63 g of a pale brown liquid.
NMR spectrum (DMSO-d_6) δ ppm:
1.57(2H,quin,J=7.5Hz),1.79(3H,s),2.34(2H,t,J=7.5Hz),2.51(4H,t,J=5Hz), 2.99(4H,t,J=5Hz),3.00-3.10(2H,m),3.67(1H, dd,J=13.5,5.5Hz),3.70-3.80(2H,m), 4.10(1H,t,J=9Hz),4.80-4.90(1H,m),7.05(1H,t,J=9Hz),7.18(1H,dd,J=9,2.5Hz), 7.46(1H,dd,J=15,2.5Hz),7.68(1H,br-s)
Mass spectrum (m/z) : 419(M^+)
Specific rotation $[\alpha]_D^{20}$ -96.2° (c = 0.1, DMSO)

Reference example 144

[0099] (R)-5-Azidomethyl-3-[3-fluoro-4-[4-(3-mesylaminopropyl)piperazin-1-yl]-phenyl]-2-oxooxazolidine
[0100] To a solution of 0.90 g of (R)-3-[4-[4-(3-aminopropyl)piperazin-1-yl]-3-fluorophenyl]-5-azidomethyl-2-oxooxazolidine in 20 ml of dried tetrahydrofuran, 0.21 ml of methanesulfonyl chloride was added under ice-cooling and with stirring, and the mixture was stirred under ice-cooling for 2 hours. The reaction solution was alkalified with aqueous sodium hydroxide, and extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (alumina, ethyl acetate : n-heptane = 1 : 1) to obtain 0.62 g of pale brown crystals.
NMR spectrum (DMSO-d_6) δ ppm:
1.65(2H,quin,J=7Hz),2.39(2H,t,J=7Hz),2.52(4H,t,J=4.5Hz),2.88(3H,s), 2.99(4H,t,J=4.5Hz),3.00(2H,t,J=7Hz),3.67

(1H,dd,J=13.5,5.5Hz),3.70-3.80(2H,m), 4.10(1H,t,J=9Hz),4.80-4.90(1H,m),6.87(1H,t,J=5.5Hz),7.05(1H,t,J=9Hz), 7.18(1H,dd,J=9,2.5Hz),7.46(1H,dd,J=14.5,2.5Hz)
IR spectrum ν (KBr) cm^{-1}: 1734,2112
Mass spectrum (m/z) : 455(M^+)
Specific rotation $[\alpha]_D^{20}$ -93.3° (c = 0.1, DMSO)

Ref rence example 145

[0101] (R)-5-Azidomethyl-3-[3-fluoro-4-(1-oxidothiomorpholin-4-yl)phenyl]-2-oxo-oxazolidine

[0102] To a solution of 5.30 g of sodium metaperiodate in 56 ml of water, a mixture of 8.00 g of (R)-5-azidomethyl-3-[3-fluoro-4-(thiomorpholin-4-yl)phenyl]-2-oxooxazolidine in 80 ml of acetonitrile and 80 ml of methanol was added dropwise, and the mixture was stirred at room temperature for 18 hours. The reaction solution was added with water, and extracted with 1,2-dichloroethane. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure to obtain 7.98 g of pale brown crystals. Recrystallization from isopropanol gave colorless prisms having the melting point of from 123.5 to 125°C.

Elemental analysis for $C_{14}H_{16}FN_5O_3S$						
Calculated %	C,	47.58;	H,	4.56;	N,	19.82
Found %	C,	47.58;	H,	4.56;	N,	19.69

Specific rotation $[\alpha]_D^{20}$ -114.1° (c = 0.1, DMSO)

Reference example 146

[0103] (R)-5-Azidomethyl-3-[3-fluoro-4-(1,1-dioxidothiomorpholin-4-yl)phenyl]-2-oxo oxazolidine

[0104] To a suspension of 5.00 g of (R)-5-azidomethyl-3-[3-fluoro-4-(thiomorpholin-4-yl)phenyl]-2-oxooxazolidine in 25 ml of water and 75 ml of acetone, 10 ml of 50 % aqueous 4-methylmorpholine-N-oxide and 3.77 g of osmium tetroxide were added under stirring at room temperature, and the mixture was stirred at the same temperature for 10 minutes. The reaction solution was added with water, and extracted with 1,2-dichloroethane. The extract was washed with saturated brine and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure to obtain 4.71 g of pale brown crystals. Recrystallization from acetone gave pale brown prisms having the melting point of from 146 to 148°C.

Elemental analysis for $C_{14}H_{16}FN_5O_4S$						
Calculated %	C,	45.52;	H,	4.37;	N,	18.96
Found %	C,	45.63;	H,	4.32;	N,	18.84

Specific rotation $[\alpha]_D^{20}$ -108.8° (c = 0.1, DMSO)

Reference example 147

[0105] (R)-1-[4-[4-(5-Azidomethyl-2-oxooxazolidin-3-yl)-2-fluorophenyl]piperazine]-carbothioamide

1) To a solution of 5.00 g of (R)-5-azidomethyl-3-[3-fluoro-4-(piperazin-1-yl)phenyl]-2-oxooxazolidine and 2.60 ml of triethylamine in 40 ml of dried tetrahydrofuran, 1.40 ml of thiophosgene was added dropwise under ice-cooling, and the mixture was stirred at the same temperature for 30 minutes. The reaction solution was added with water, and extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure to obtain 4.32 g of (R)-5-azidomethyl-3-[4-(4-chlorothiocarbonylpiperazin-1-yl)-3-fluorophenyl]-2-oxooxazolidine as brown crystals.
2) A solution of 4.32 g of the crystals obtained in 1) in 43 ml of dried tetrahydrofuran was stirred with bubbling of ammonia gas at room temperature for 3 hours. The reaction solution was concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, 1,2-dichloroethane : methanol = 20 : 1) to obtain 2.95 g of pale brown crystals.
NMR spectrum (DMSO-d_6) δ ppm:
2.99(4H,t,J=5Hz),3.66(1H,dd,J=13.5,5.5Hz),3.70-3.80(2H,m),3.91(4H,t,J=5Hz), 4.11(1H,t,J=9Hz),4.80-4.90(1H, m),7.09(1H,t,J=9Hz),7.20(1H,dd,J=9,2.5Hz), 7.39(2H,br-s),7.50(1H,dd,J=14.5,2.5Hz)

IR spectrum ν (KBr) cm^{-1}: 1738,2108,3184,3286,3424
Specific rotation $[\alpha]_D^{20}$ -109.1° (c = 0.1, DMSO)

Reference example 148

[0106] (R)-N,N-Dimethyl-1-[4-[4-(5-azidomethyl-2-oxooxazolidin-3-yl)-2-fluorophenyl]piperazine]carbothioamide

[0107] To a solution of 5.00 g of the crystals obtained by the method of Reference example 147-1) in 20 ml of dried tetrahtdrofuran, 10 ml of 50% aqueous dimethylamine was added at room temperature, and the mixture was stirred at the same temperature for 18 hours. The reaction solution was concentrated under reduced pressure, and the residue was washed successively with water and ethanol to obtain 4.25 g of pale brown crystals. Recrystallization from acetonitrile gave pale brown prisms having the melting point of from 160 to 162°C.

Elemental analysis for $C_{17}H_{22}FN_7O_2S$					
Calculated %	C,	50.11;	H,	5.44;	N, 24.06
Found %	C,	50.38;	H,	5.44;	N, 23.95

Specific rotation $[\alpha]_D^{20}$ -101.7° (c = 0.1, DMSO)

Reference example 149

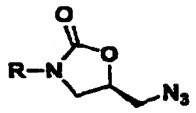
[0108] O-Methyl (R)-1-[4-[4-(5-azidomethyl-2-oxooxazolidin-3-yl)-2-fluorophenyl]-piperazine]thiocarboxylate

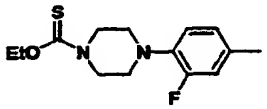
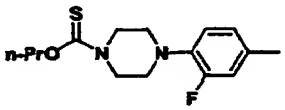
[0109] A solution of 5.00 g of the crystals obtained by the method of Reference example 147-1) in 50 ml of methanol was stirred with heating to 60°C for 30 minutes, and then stirred at room temperature for 1 hour. The precipitated crystals were collected by filtration, and washed with diisopropyl ether to obtain 4.00 g of pale brown crystals. Recrystallization from methanol gave pale brown needles having the melting point of from 138 to 139°C.

Elemental analysis for $C_{16}H_{19}FN_6O_3S$						
Calculated %	C,	48.72;	H,	4.86;	N,	21.31
Found %	C,	48.79;	H,	4.84;	N,	20.94

Specific rotation $[\alpha]_D^{20}$ -105.4° (c = 0.1, DMSO)

[0110] The compounds of Reference examples 150 through 151 were obtained in the same manner as in Reference example 149.



Reference example	R	Physical properties [recrystallization solvent]
150		brown crystals [EtOH] mp,122.5~125.5℃ Elemental analysis for $C_{17}H_{21}FN_6O_3S$ Calcd. % : C,49.99;H,5.18;N,20.58 Found % : C,50.16;H,5.06;N,20.54 Specific rotation $[\alpha]_D^{20}$-104.5° (c=0.1,DMSO)
151		pale brown crystals [MeOH] mp,122.5~124.5℃ Elemental analysis for $C_{18}H_{23}FN_6O_3S$ Calcd. % : C,51.17;H,5.49;N,19.89 Found % : C,51.09;H,5.26;N,19.78 Specific rotation $[\alpha]_D^{20}$-100.3° (c=0.1,DMSO)

Reference example 152

[0111] Methyl (R)-1-[4-[4-(5-azidomethyl-2-oxooxazolidin-3-yl)-2-fluorophenyl]-piperazine]carbodithioate

[0112] To a solution of 5.00 g of (R)-5-azidomethyl-3-[3-fluoro-4-(piperazin-1-yl)-phenyl]-2-oxooxazolidine and 2.20 ml of triethylamine in 50 ml of dried tetrahydrofuran, 2.00 ml of carbon disulfide was added dropwise under ice-cooling, and the mixture was stirred at room temperature for 18 hours. Furthermore, the mixture was added with 1.00 ml of methyl iodide under ice-cooling, and stirred at the same temperature for 30 minutes. The reaction solution was added with water, and extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was washed with ethanol to obtain 5.96 g of colorless crystals. Recrystallization from acetonitrile gave pale brown prisms having the melting point of from 139.5 to 140°C.

Elemental analysis for $C_{16}H_{19}FN_6O_2S_2$						
Calculated %	C,	46.81;	H,	4.67;	N,	20.47
Found %	C,	46.96;	H,	4.68;	N,	20.41

Specific rotation $[\alpha]_D^{20}$ -104.6° (c = 0.1, DMSO)

Reference example 153

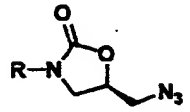
[0113] (R)-N-Methyl-1-[4-[4-(5-azidomethyl-2-oxooxazolidin-3-yl)-2-fluorophenyl]-piperazine]carbothioamide

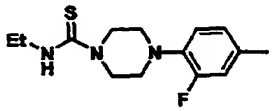
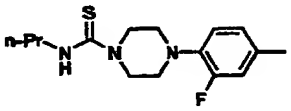
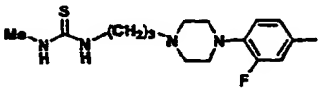
[0114] To a solution of 3.00 g of (R)-5-azidomethyl-3-[3-fluoro-4-(piperazin-1-yl)-phenyl]-2-oxooxazolidine in 30 ml of dried tetrahydrofuran, 0.71 ml of methyl isothiocyanate was added under ice-cooling and with stirring, and the mixture was stirred at the same temperature for 1 hour. The reaction solution was added with water, and the precipitated crystals were collected by filtration, and then washed with diisopropyl ether to obtain 3.63 g of colorless crystals. Recrystallization from ethyl acetate gave colorless needles having the melting point of from 156.5 to 158°C.

Elemental analysis for $C_{16}H_{20}FN_7O_2S$						
Calculated %	C,	48.84;	H,	5.12;	N,	24.92
Found %	C,	48.70;	H,	5.09;	N,	24.88

Specific rotation $[\alpha]_D^{20}$ -111.7° (c = 0.1, DMSO)

[0115] The compounds of Reference examples 154 through 156 were obtained in the same manner as in Reference example 153.



Reference example	R	Physical properties [recrystallization solvent]
154		colorless prisms[EtOH] mp,174~175.5℃ Elemental analysis for $C_{17}H_{22}FN_7O_2S$ Calcd. % : C,50.11;H,5.44;N,24.06 Found % : C,50.16;H,5.28;N,23.98 Specific rotation $[\alpha]_D^{20}$-108.8° (c=0.1,DMSO)
155		colorless crystals[EtOH] mp,172.5~174.5℃ Elemental analysis for $C_{18}H_{24}FN_7O_2S$ Calcd. % : C,51.29;H,5.74;N,23.26 Found % : C,51.49;H,5.72;N,23.08 Specific rotation $[\alpha]_D^{20}$-104.0° (c=0.1,DMSO)
156		colorless crystals NMR(DMSO-d_6) δ ppm:1.68(2H,quin,J=7 Hz),2.37(2H,t,J=7Hz),2.53(4H,t,J=5H z),2.83(3H,d,J=4.5Hz),3.00(4H,t,J=5H z),3.30-3.45(2H,m),3.67(1H,dd,J=13.5, 5.5Hz),3.74(1H,dd,J=13.5,3.5Hz),3.74(1H,dd,J=9,6Hz),4.11(1H,t,J=9Hz),4.80 -4.90(1H,m),7.05(1H,t,J=9Hz),7.18(1H ,dd,J=9,2.5Hz),7.31(1H,br-s),7.37(1H, br-s),7.46(1H,dd,J=15,2.5Hz) IR ν (KBr) cm^{-1}:1764,2104,3240 Specific rotation $[\alpha]_D^{20}$-89.8° (c=0.1,DMSO)

Reference example 157

[0116] (R)-3-[4-[4-(5-Azidomethyl-2-oxooxazolidin-3-yl)-2-fluorophenyl]piperazin-1-yl]propyl isothiocyanate

[0117] To a solution of 2.00 g of (R)-3-[4-[4-(3-aminopropyl)piperazin-1-yl]-3-fluorophenyl]-5-azidomethyl-2-oxooxazolidine and 0.74 ml of triethylamine in 20 ml of dried tetrahydrofuran, 0.64 ml of carbon disulfide was added dropwise under ice-cooling, and the mixture was stirred at the same temperature for 5 hours. The mixture was added with 0.51 ml of ethyl chlorocarbonate, and further stirred at the same temperature for 1.5 hours. The reaction solution was added with water, and extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate) to obtain 0.85 g of a brown liquid.

NMR spectrum (DMSO-d_6) δ ppm :

1.84(2H,quin,J=6.5Hz),2.43(2H,t,J=6.5Hz),2.53(4H,t,J=4.5Hz),3.00(4H,t,J=4.5Hz), 3.60-3.80(5H,m),4.11(1H,t,J=9Hz), 4.80-4.90(1H,m),7.05(1H,t,J=9Hz), 7.18(1H,dd,J=9,2.5Hz),7.46(1H,dd,J=14.5,2.5Hz)

IR spectrum ν (liq.) cm^{-1}: 1754,2112,2184

Mass spectrum (m/z) : 419(M^+)

Specific rotation $[\alpha]_D^{20}$ -89.1° (c = 0.1, DMSO)

Reference example 158

[0118] Methyl (R)-N-[3-[4-[4-(5-azidomethyl-2-oxooxazolidin-3-yl)-2-fluorophenyl]-piperazin-1-yl]propyl]thiocarbamate

[0119] To 25 ml of dried methanol, 0.87 g of 60 % sodium hydride was added under ice-cooling and with stirring, and the mixture was stirred at room temperature for 30 minutes. Then, the mixture was added with a solution of 4.56 g of (R)-3-[4-[4-(5-azidomethyl-2-oxooxazolidin-3-yl)-2-fluorophenyl]piperazin-1-yl]propyl isothiocyanate in 30 ml of dried methanol-dried tetrahydrofuran (2 : 1), and stirred at room temperature for 1.5 hours. The reaction mixture was acidified with ice water and 10 % hydrochloric acid, and extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate : n-heptane = 2 : 1) to obtain 4.32 g of a brown liquid.

NMR spectrum (DMSO-d_6) δ ppm:
1.60-1.75(2H,m),2.39(2H,t,J=6.5Hz),2.53(4H,t,J=5Hz),3.02(4H,t,J=5Hz), 3.40-3.50(2H,m),3.65(1H,dd, J=13.5,5.5Hz),3.72(1H,dd,J=13.5,3.5Hz), 3.74(1H,dd,J=9,6Hz),3.87(3H,s),4.10(1H,t,J=9Hz),4.80-4.90(1H,m),7.03 (1H,t,J=9Hz), 7.17(1H,dd,J=9,2.5Hz),7.41(1H,dd,J=15.5,2.5Hz),8.77(1H,br-s)
IR spectrum ν (liq.) cm^{-1}: 1748,2112,3284
Mass spectrum (m/z) : 451(M^+)
Specific rotation $[\alpha]_D^{20}$ -85.5° (c = 0.1, DMSO)

Reference example 159

[0120] (R)-5-Azidomethyl-3-[3-fluoro-4-(4-oxopiperidin-1-yl)phenyl]-2-oxooxazolidine

[0121] A suspension of 1.45 g of (R)-5-azidomethyl-3-[4-(1,4-dioxa-8-azaspiro[4.5]-decan-8-yl)-3-fluorophenyl]-2-oxooxazolidine and 1.10 g of p-toluenesulfonic acid in 60 ml of acetone-water (1:1) was heated under reflux for 18 hours. The solvent was evaporated under reduced pressure, and the residue was neutralized with aqueous sodium hydrogencarbonate, and then extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate : n-heptane = 1 : 1) to obtain 1.20 g of colorless crystals. Recrystallization from ethanol gave colorless crystals having the melting point of from 99.5 to 101°C.

Elemental analysis for $C_{15}H_{16}FN_5O_3$						
Calculated %	C,	54.05;	H,	4.84;	N,	21.01
Found %	C,	54.02;	H,	4.87;	N,	21.18

Specific rotation $[\alpha]_D^{20}$ -118.4° (c = 0.1, DMSO)

Reference example 160

[0122] (R)-5-Azidomethyl-3-[3-fluoro-4-(4-hydroxyiminopiperidin-1-yl)phenyl]-2-oxo-oxazolidine

[0123] A suspension of 6.75 g of (R)-5-azidomethyl-3-[3-fluoro-4-(4-oxopiperidin-1-yl)phenyl]-2-oxooxazolidine, 1.55 g of hydroxylamine hydrochloride and 3.66 g of sodium acetate in 135 ml of methanol was stirred at room temperature for 1 hour. The reaction solution was added with water, and the precipitated crystals were collected by filtration, and then washed with diisopropyl ether to obtain 6.52 g of pale brown crystals. Recrystallization from ethyl acetate gave colorless prisms having the melting point of from 155 to 156°C.

Elemental analysis for $C_{15}H_{17}FN_6O_3$						
Calculated %	C,	51.72;	H,	4.92;	N,	24.13
Found %	C,	51.72;	H,	4.81;	N,	24.22

Specific rotation $[\alpha]_D^{20}$ -131.7° (c = 0.1, DMSO)

Reference example 161

[0124] (R)-5-Azidomethyl-3-[3-fluoro-4-(4-thiobenzoylpiperazin-1-yl)phenyl]-2-oxo-oxazolidine

[0125] To a solution of 2.00 g of (R)-5-azidomethyl-3-[3-fluoro-4-(piperazin-1-yl)-phenyl]-2-oxooxazolidine and 1.97 ml of triethylamine in 20 ml of dried 1,2-dichloroethane, 10.0 g of thiobenzoyl chloride was added dropwise under ice-cooling and with stirring, and the mixture was stirred at the same temperature for 1 hour. The reaction solution was added with water, and extracted with 1,2-dichloroethane. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate : n-heptane = 1 : 4) to obtain 3.30 g of a green liquid.

NMR spectrum ($CDCl_3$) δ ppm:
3.04(2H,t,J=5Hz),3.27(2H,t,J=5Hz),3.59(1H,dd,J=13.5,4.5Hz), 3.71(1H,dd,J=13.5,4.5Hz),3.76(2H,t,J=5Hz),3.88(1H, dd,J=8.5,6Hz), 4.05(1H,t,J=8.5Hz),4.61(2H,t,J=5Hz),4.75-4.80(1H,m),6.94(1H,t,J=9Hz), 7.13(1H,d,J=9Hz),7.30-7.40 (5H,m),7.48(1H,dd,J=14,2.5Hz)
Mass spectrum (m/z) : 440(M^+)
Specific rotation $[\alpha]_D^{20}$ -85.3° (c = 0.1, DMSO)

Ref rence example 162

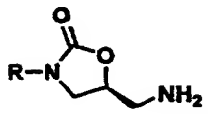
[0126] (S)-5-Aminomethyl-2-oxo-3-[4-(thiomorpholin-4-yl)phenyl]oxazolidine

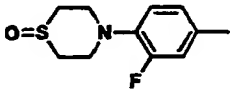
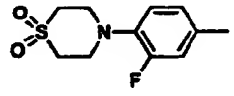
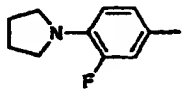
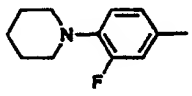
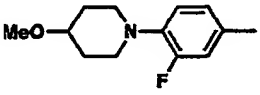
[0127] A solution of 8.50 g of (R)-5-azidomethyl-2-oxo-3-[4-(thiomorpholin-4-yl)-phenyl]oxazolidine and 7.68 g of triphenylphosphine in 130 ml of dried tetrahydrofuran was stirred at room temperature for 15 hours. Furthermore, the mixture was added with 4.8 ml of water, and stirred with heating to 40°C for 14 hours. The reaction solution was cooled, then added with 100 ml of water, acidified with 10 % hydrochloric acid, and then extracted with diethyl ether. The aqueous layer was alkalified with potassium carbonate, and extracted with a mixture of dichloromethane-methanol (30 : 1). The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure to obtain 6.88 g of colorless crystals. Recrystallization from ethyl acetate gave colorless crystals having the melting point of from 119.5 to 121°C.

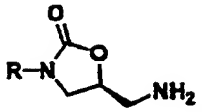
Elemental analysis for $C_{14}H_{19}N_3O_2S$						
Calculated %	C,	57.31;	H,	6.53;	N,	14.32
Found %	C,	57.36;	H,	6.45;	N,	14.06

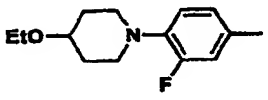
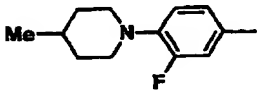
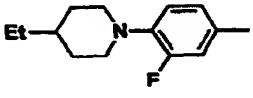
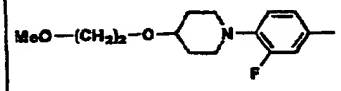
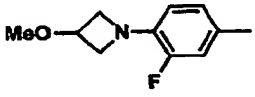
Specific rotation $[\alpha]_D^{20}$ -35.9° (c = 0.1, DMSO)

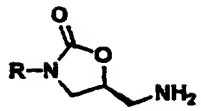
[0128] The compounds of Reference examples 163 through 212 were obtained in the same manner as in Reference example 162.

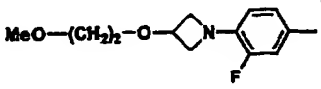
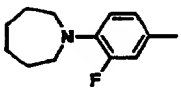
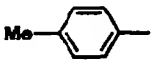
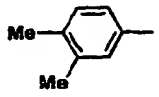


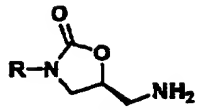
Reference example	R	Physical properties [recrystallization solvent]
163		pale brown crystals NMR($CDCl_3$) δ ppm:1.36(2H,br-s),2.95-3.00(5H,m),3.13(1H,dd,J=13.5,4Hz),3.20-3.30(2H,m),3.70-3.80(2H,m),3.83(1H,dd,J=8.5,7Hz),4.01(1H,t,J=8.5Hz),4.60-4.70(1H,m),7.03(1H,t,J=9Hz),7.12(1H,dd,J=9,2Hz),7.54(1H,dd,J=14,2Hz) IR ν (KBr) cm^{-1}:1750,3400 MS(m/z):327(M^+) Specific rotation $[\alpha]_D^{20}$-39.0° (c=0.1,DMSO)
164		colorless prisms[EtOH] mp,162～163℃ Elemental analysis for $C_{14}H_{18}FN_3O_4S$ Calcd. % : C,48.97;H,5.28;N,12.24 Found % : C,48.92;H,5.28;N,12.08 Specific rotation $[\alpha]_D^{20}$-32.9° (c=0.1,DMSO)
165		colorless crystals[AcOEt] mp,100～101.5℃ Elemental analysis for $C_{14}H_{18}FN_3O_2$ Calcd. % : C,60.20;H,6.50;N,15.04 Found % : C,60.16;H,6.44;N,15.18 Specific rotation $[\alpha]_D^{20}$-38.9° (c=0.1,DMSO)
166		pale brown crystals[i-PrOH-i-Pr_2O] mp,90～92℃ Elemental analysis for $C_{15}H_{20}FN_3O_2$ Calcd. % : C,61.42;H,6.87;N,14.32 Found % : C,61.16;H,6.56;N,14.40 Specific rotation $[\alpha]_D^{20}$-36.1° (c=0.1,DMSO)
167		colorless needles[AcOEt-i-Pr_2O] mp,102～102.5℃ Elemental analysis for $C_{16}H_{22}FN_3O_3$ Calcd. % : C,59.43;H,6.86;N,12.99 Found % : C,59.13;H,6.72;N,12.89 Specific rotation $[\alpha]_D^{20}$-35.0° (c=0.1,DMSO)

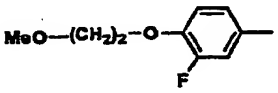
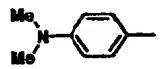
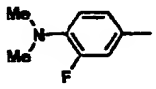
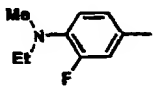


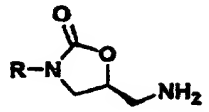
Reference example	R	Physical properties [recrystallization solvent]
168		pale brown crystals [i-PrOH] mp,85～86.5℃ Elemental analysis for $C_{17}H_{24}FN_3O_3$ Calcd. % : C,60.52;H,7.17;N,12.45 Found % : C,60.28;H,7.42;N,12.42 Specific rotation [α]$_D^{20}$-29.1° (c=0.1,DMSO)
169		colorless needles [AcOEt-i-Pr_2O] mp,111.5～113℃ Elemental analysis for $C_{18}H_{22}FN_3O_2$ Calcd. % : C,62.52;H,7.21;N,13.67 Found % : C,62.43;H,7.43;N,13.59 Specific rotation [α]$_D^{20}$-35.9° (c=0.1,DMSO)
170		colorless plates [i-PrOH] mp,113～114℃ Elemental analysis for $C_{17}H_{24}FN_3O_2$ Calcd. % : C,63.53;H,7.53;N,13.07 Found % : C,63.34;H,7.84;N,12.97 Specific rotation [α]$_D^{20}$-35.9° (c=0.1,DMSO)
171		pale brown crystals NMR(DMSO-d_6) δ ppm:1.52(2H,br-s),1.55-1.65 (2H,m),1.90-2.00(2H,m),2.70-2.85(3H,m),2.85(1H,dd,J=13.5,5Hz),3.15-3.25(2H,m),3.27(3H,s),3.40-3.50(1H,m),3.45(2H,t,J=5Hz),3.56(2H,t,J=5Hz),3.81(1H,dd,J=9,6.5Hz),4.01(1H,t,J=9Hz),4.55-4.65(1H,m),7.05(1H,t,J=9Hz),7.17(1H,dd,J=9,2.5Hz),7.46(1H,dd,J=15,2.5Hz) MS(m/z):367(M^+) Specific rotation [α]$_D^{20}$-30.1° (c=0.1,DMSO)
172		pale brown crystals [AcOEt] mp,105～106.5℃ Elemental analysis for $C_{14}H_{18}FN_3O_3$ Calcd. % : C,56.94;H,6.14;N,14.23 Found % : C,56.68;H,5.92;N,14.00 Specific rotation [α]$_D^{20}$-36.1° (c=0.1,DMSO)

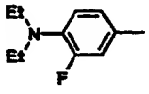
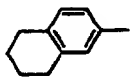
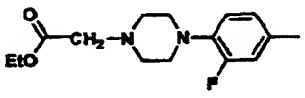
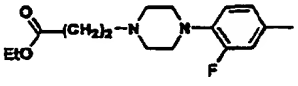


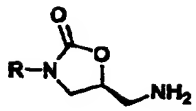
Reference example	R	Physical properties [recrystallization solvent]
173		brown liquid NMR(DMSO-d_6) δ ppm:1.54(2H,br-s),2.79(1H, dd,J=13.5,5Hz),2.84(1H,dd,J=13.5,5Hz),3.26(3H,s),3.45(2H,t,J=4.5Hz),3.53(2H,t,J=4.5Hz),3.60-3.65(2H,m),3.78(1H,dd,J=8.5,6.5Hz),3.98(1H,t,J=8.5Hz),4.05-4.15(2H,m),4.35-4.45(1H,m),4.50-4.60(1H,m),6.57(1H,t,J=8.5Hz),7.12(1H,dd,J=8.5,2Hz),7.38(1H,dd,J=14.5,2Hz) IR ν (liq.) cm^{-1}:1744,3384 MS(m/z):339(M^+) Specific rotation [α]$_D^{20}$-27.9° (c=0.1,DMSO)
174		colorless crystals[AcOEt-i-Pr_2O] mp,87～87.5℃ Elemental analysis for $C_{16}H_{22}FN_3O_2$ Calcd. % : C,62.52;H,7.21;N,13.67 Found % : C,62.23;H,7.28;N,13.51 Specific rotation [α]$_D^{20}$-44.0° (c=0.1,DMSO)
175		colorless amorphous solid NMR(DMSO-d_6) δ ppm:2.27(3H,s),2.80(1H,dd, J=13.5,5Hz),2.85(1H,dd,J=13.5,5Hz),3.07(2H,br-s),3.82(1H,dd,J=8.5,6Hz),4.02(1H,t,J=8.5Hz),4.53-4.61(1H,m),7.18(2H,d,J=8.5Hz),7.43(2H,d,J=8.5Hz) IR ν (KBr) cm^{-1}:1748,3356 MS(m/z):206(M^+) Specific rotation [α]$_D^{20}$-38.1° (c=0.1,DMSO)
176		pale yellow crystals NMR(DMSO-d_6) δ ppm:1.60(2H,br-s),2.19(3H, s),2.22(3H,s),2.80(1H,dd,J=13.5,5.5Hz),2.85(1H,dd,J=13.5,5.5Hz),3.81(1H,dd,J=9,6Hz),4.01(1H,t,J=9Hz),4.50-4.60(1H,m),7.11(1H,d,J=8.5Hz),7.27(1H,dd,J=8.5,2.5Hz),7.32(1H,d,J=2.5Hz) IR ν (KBr) cm^{-1}:1730,3420 MS(m/z):220(M^+) Specific rotation [α]$_D^{20}$-37.0° (c=0.1,DMSO)

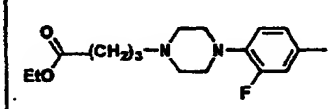
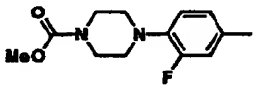
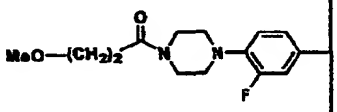
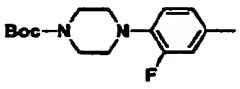


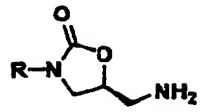
Reference example	R	Physical properties [recrystallization solvent]
177		pale yellow crystals NMR($CDCl_3$) δ ppm:1.31(2H,br-s),2.98(1H,dd,J=13.5,4.5Hz),3.11(1H,dd,J=13.5,4.5Hz),3.45(3H,s),8.76(2H,t,J=4.5Hz),3.82(1H,dd,J=8.5,6.5Hz),4.00(1H,t,J=8.5Hz),4.18(2H,t,J=4.5Hz),4.60-4.70(1H,m),7.00(1H,t,J=9Hz),7.10-7.20(1H,m),7.47(1H,dd,J=13,3Hz) IR ν (KBr) cm^{-1}:1746,3328,3396 MS(m/z):284(M^+) Specific rotation $[\alpha]_D^{20}$-33.0° (c=0.1,DMSO)
178		pale brown needles[AcOEt-i-Pr_2O] mp,91.5~92°C Elemental analysis for $C_{12}H_{17}N_3O_2$ Calcd. % : C,61.26;H,7.28;N,17.86 Found % : C,60.90;H,7.16;N,17.60 Specific rotation $[\alpha]_D^{20}$-32.9° (c=0.1,DMSO)
179		reddish brown crystals NMR(DMSO-d_6) δ ppm:1.88(2H,br-s),2.74(6H,s),2.79(1H,dd,J=13.5,5Hz),2.85(1H,dd,J=13.5,5Hz),3.80(1H,dd,J=9,6Hz),4.00(1H,t,J=9Hz),4.50-4.65(1H,m),6.97(1H,t,J=8.5Hz),7.16(1H,dd,J=8.5,2.5Hz),7.44(1H,dd,J=15.5,2.5Hz) IR ν (KBr) cm^{-1}:1732,3336,3372 MS(m/z):253(M^+) Specific rotation $[\alpha]_D^{20}$-45.0° (c=0.1,DMSO)
180		colorless crystals[AcOEt-i-Pr_2O] mp,51~52°C Elemental analysis for $C_{13}H_{18}FN_3O_2$ Calcd. % : C,58.41;H,6.79;N,15.72 Found % : C,58.42;H,6.78;N,15.52 Specific rotation $[\alpha]_D^{20}$-45.8° (c=0.1,DMSO)

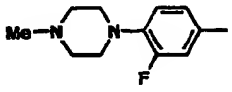
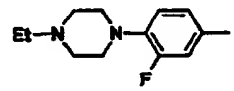
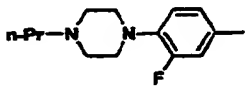
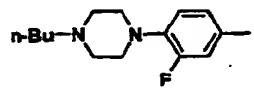


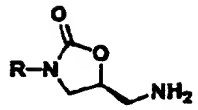
Reference example	R	Physical properties [recrystallization solvent]
181		brown liquid NMR(DMSO-d6) δ ppm:0.99(6H,t,J=7.5Hz),1.55(2H,br-s),2.80(1H,dd,J=14,5Hz),2.85(1H,dd,J=14,5Hz),3.11(4H,q,J=7.5Hz),3.81(1H,dd,J=9,6.5Hz),4.02(1H,t,J=9Hz),4.55-4.65(1H,m),7.02(1H,t,J=9.5Hz),7.17(1H,dd,J=9.5,2.5Hz),7.43(1H,dd,J=15.5,2.5Hz) IR ν (liq.) cm^{-1}:1750,3392 MS(m/z):281(M^+) Specific rotation [α]$_D^{20}$-33.3° (c=0.1,DMSO)
182		colorless prisms[i-PrOH-n-Hexane] mp,81~82.5℃ Elemental analysis for $C_{14}H_{18}N_2O_2$ Calcd. % : C,68.27;H,7.37;N,11.37 Found % : C,68.03;H,7.53;N,11.31 Specific rotation [α]$_D^{20}$-36.0° (c=0.1,DMSO)
183		pale brown crystals NMR(DMSO-d6) δ ppm:1.21(3H,t,J=7.5Hz),2.15(2H,br-s),2.68(4H,t,J=4.5Hz),2.80(1H,dd,J=13.5,5Hz),2.85(1H,dd,J=13.5,5Hz),2.99(4H,t,J=4.5Hz),3.26(2H,s),3.81(1H,dd,J=9,6.5Hz),4.02(1H,t,J=9Hz),4.11(2H,q,J=7.5Hz),4.55-4.65(1H,m),7.05(1H,t,J=9Hz),7.18(1H,dd,J=9,2.5Hz),7.47(1H,dd,J=14.5,2.5Hz) IR ν (KBr) cm^{-1}:1740,3388 MS(m/z):380(M^+) Specific rotation [α]$_D^{20}$-34.0° (c=0.1,DMSO)
184		colorless crystals[i-PrOH-i-Pr_2O] mp,88~88.5℃ Elemental analysis for $C_{19}H_{27}FN_4O_4$ Calcd. % : C,57.85;H,6.90;N,14.20 Found % : C,57.57;H,7.15;N,14.06 Specific rotation [α]$_D^{20}$-30.0° (c=0.1,DMSO)

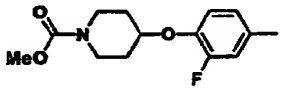
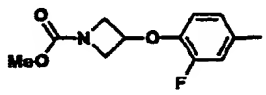
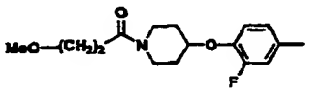


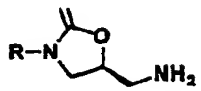
Reference example	R	Physical properties [recrystallization solvent]
185		pale brown crystals NMR(DMSO-d_6) δ ppm:1.19(3H,t,J=7.5Hz),1.71(2H,quin,J=7.5Hz),1.71(2H,br-s),2.31(2H,t,J=7.5Hz),2.34(2H,t,J=7.5Hz),2.50(4H,t,J=5Hz),2.80(1H,dd,J=13.5,5Hz),2.85(1H,dd,J=13.5,5Hz),2.97(4H,t,J=5Hz),3.81(1H,dd,J=9,6.5Hz),4.01(1H,t,J=9Hz),4.06(2H,q,J=7.5Hz),4.55-4.65(1H,m),7.03(1H,t,J=9Hz),7.18(1H,dd,J=9,2.5Hz),7.47(1H,dd,J=15.5,2.5Hz) MS(m/z):408(M^+) Specific rotation $[\alpha]_D^{20}$-26.9° (c=0.1,DMSO)
186		colorless prisms[i-PrOH] mp,109~111℃ Elemental analysis for $C_{16}H_{21}FN_4O_4$ Calcd. % : C,54.54;H,6.01;N,15.90 Found % : C,54.31;H,6.00;N,15.83 Specific rotation $[\alpha]_D^{20}$-29.7° (c=0.07,DMSO)
187		pale yellow crystals[i-PrOH] mp,134~135℃ Elemental analysis for $C_{18}H_{25}FN_4O_4$ Calcd. % : C,56.83;H,6.62;N,14.73 Found % : C,56.86;H,6.74;N,14.66 Specific rotation $[\alpha]_D^{20}$-35.0° (c=0.1,DMSO)
188		colorless crystals[AcOEt-i-Pr_2O] mp,138~139℃ Elemental analysis for $C_{19}H_{27}FN_4O_4$ Calcd. % : C,57.85;H,6.90;N,14.20 Found % : C,57.75;H,7.14;N,14.06 Specific rotation $[\alpha]_D^{20}$-26.9° (c=0.1,DMSO)

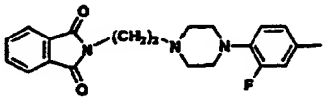
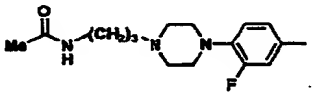
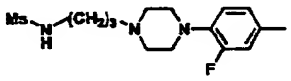


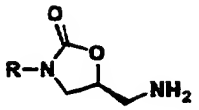
Reference example	R	Physical properties [recrystallization solvent]
189		pale yellow crystals NMR(DMSO-d_6) δ ppm:1.89(2H,br-s),2.22(3H,s),2.46(4H,t,J=5Hz),2.79(1H,dd,J=14,5Hz),2.84(1H,dd,J=14,5Hz),2.98(4H,t,J=5Hz),3.81(1H,dd,J=9,6Hz),4.01(1H,t,J=9Hz),4.54-4.61(1H,m),7.03(1H,t,J=8.5Hz),7.18(1H,dd,J=8.5,2Hz),7.46(1H,dd,J=15.5,2Hz) IR ν (KBr) cm^{-1}:1734,3328,3372 MS(m/z):308(M^+) Specific rotation [α]$_D^{20}$-34.0° (c=0.1,DMSO)
190		colorless needles[AcOEt-i-Pr_2O] mp,104～105.5℃ Elemental analysis for $C_{16}H_{23}FN_4O_2$ Calcd. % : C,59.61;H,7.19;N,17.38 Found % : C,59.46;H,7.17;N,17.37 Specific rotation [α]$_D^{20}$-37.0° (c=0.1,DMSO)
191		pale brown crystals[AcOEt-i-Pr_2O] mp,93～95℃ Elemental analysis for $C_{17}H_{25}FN_4O_2$ Calcd. % : C,60.70;H,7.49;N,16.65 Found % : C,60.47;H,7.38;N,16.55 Specific rotation [α]$_D^{20}$-37.9° (c=0.1,DMSO)
192		pale yellow crystals[i-PrOH-i-Pr_2O] mp,98～100℃ Elemental analysis for $C_{18}H_{27}FN_4O_2 \cdot 2/5H_2O$ Calcd. % : C,60.45;H,7.83;N,15.67 Found % : C,60.62;H,7.81;N,15.46 Specific rotation [α]$_D^{20}$-34.1° (c=0.1,DMSO)

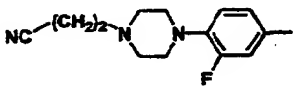
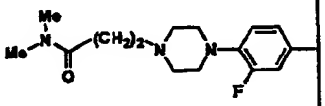
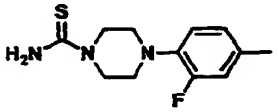
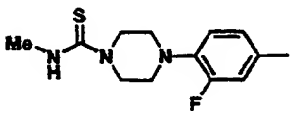


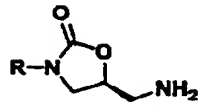
Reference example	R	Physical properties [recrystallization solvent]
193		pale yellowish brown liquid NMR(DMSO-d_6) δ ppm:1.54-1.62(2H,m), 1.82(2H,br-s),1.85-1.92(2H,m),2.81(1H ,dd,J=14,5Hz),2.86(1H,dd,J=14,5Hz),3 .22-3.29(2H,m),3.60(3H,s),3.64-3.70(2 H,m),3.82(1H,dd,J=9,6Hz),4.03(1H,t,J =9Hz),4.45-4.52(1H,m),4.57-4.63(1H, m),7.22(1H,dd,J=9,2.5Hz),7.25(1H,t,J =9Hz),7.54(1H,dd,J=13.5,2.5Hz) IR ν (liq.) cm^{-1}:1688,1748,3368 MS(m/z):367(M^+) Specific rotation [α]$_D^{20}$-26.0° (c=0.1,DMSO)
194		colorless prisms[AcOEt] mp,119.5～122℃ Elemental analysis for $C_{15}H_{18}FN_3O_5 \cdot 1/6H_2O$ Calcd. % : C,52.63;H,5.40;N,12.28 Found % : C,52.49;H,5.29;N,12.27 Specific rotation [α]$_D^{20}$-30.9° (c=0.1,DMSO)
195		pale yellow liquid NMR(DMSO-d_6) δ ppm:1.50-1.70(2H,m), 1.80-2.00(2H,m),1.91(2H,br-s),2.57(2H ,t,J=6.5Hz),2.81(1H,dd,J=13.5,5Hz),2. 86(1H,dd,J=13.5,5Hz),3.20-3.40(2H,m),3.23(3H,s),3.56(2H,t,J=6.5Hz),3.82(1 H,dd,J=9,6Hz),4.03(1H,t,J=9Hz),4.45- 4.55(1H,m),4.55-4.65(1H,m),7.22(1H,d d,J=9,2.5Hz),7.25(1H,t,J=9Hz),7.54(1 H,dd,J=13.5,2.5Hz) IR ν (liq.) cm^{-1}:1634,1750,3464 MS(m/z):395(M^+) Specific rotation [α]$_D^{20}$-34.7° (c=0.1,DMSO)

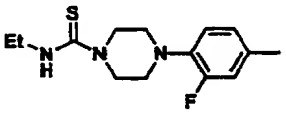
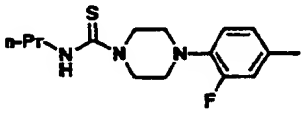
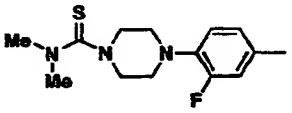
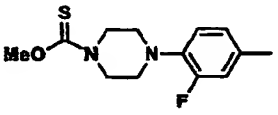
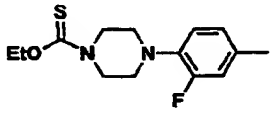


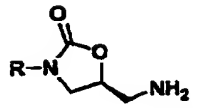
Reference example	R	Physical properties [recrystallization solvent]
196		pale brown crystals NMR(DMSO-d_6) δ ppm:2.45-2.65(6H,m),2.90-3.10(4H,m),3.30-3.40(3H,m),3.50-3.65(2H,m),4.00-4.15(1H,m),4.75-4.85(1H,m),7.00(1H,t,J=9Hz),7.10-7.25(2H,m),7.35-7.55(4H,m) IR ν (KBr) cm^{-1}:1712,1750,3424 MS(m/z):467(M^+) Specific rotation $[\alpha]_D^{20}$-30.0° (c=0.1,DMSO)
197		pale brown amorphous solid NMR(DMSO-d_6) δ ppm:1.57(2H,quin,J=7.5Hz),1.62(2H,br-s),1.79(3H,s),2.34(2H,t,J=7.5Hz),2.51(4H,t,J=5Hz),2.80(1H,dd,J=13.5,5Hz),2.85(1H,dd,J=13.5,5Hz),2.98(4H,t,J=5Hz),3.00-3.10(2H,m),3.81(1H,dd,J=9,6.5Hz),4.01(1H,t,J=9Hz),4.55-4.65(1H,m),7.04(1H,t,J=9Hz),7.18(1H,dd,J=9,2.5Hz),7.47(1H,dd,J=15.5,2.5Hz),7.68(1H,br-s) IR ν (KBr) cm-1:1724,1744,3304 MS(m/z):393(M^+) Specific rotation $[\alpha]_D^{20}$-28.9° (c=0.1,DMSO)
198		pale brown crystals NMR(DMSO-d_6) δ ppm:1.65(2H,quin,J=7Hz),1.77(2H,br-s),2.39(2H,t,J=7Hz),2.52(4H,t,J=4.5Hz),2.80(1H,dd,J=13.5,5Hz),2.85(1H,dd,J=13.5,5Hz),2.88(3H,s),2.98(4H,t,J=4.5Hz),3.00(2H,t,J=7Hz),3.81(1H,dd,J=9,6.5Hz),4.02(1H,t,J=9Hz),4.55-4.65(1H,m),6.87(1H,br-s),7.04(1H,t,J=9Hz),7.18(1H,dd,J=9,2.5Hz),7.47(1H,dd,J=14.5,2.5Hz) IR ν (KBr) cm^{-1}:1726,3276 MS(m/z):429(M^+) Specific rotation $[\alpha]_D^{20}$-23.0° (c=0.1,DMSO)

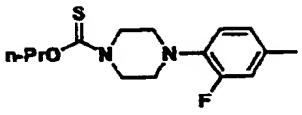
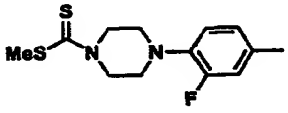
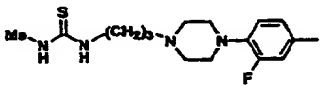


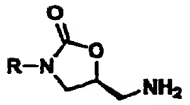
Reference example	R	Physical properties [recrystallization solvent]
199		colorless needles [i-PrOH] mp,115.5～117℃ Elemental analysis for $C_{17}H_{22}FN_5O_2$ Calcd. % : C,58.78;H,6.38;N,20.16 Found % : C,58.60;H,6.38;N,20.09 Specific rotation $[\alpha]_D^{20}$-36.9° (c=0.1,DMSO)
200		colorless crystals [AcOEt] mp,142～144℃ Elemental analysis for $C_{19}H_{28}FN_5O_3$ Calcd. % : C,58.00;H,7.17;N,17.80 Found % : C,57.82;H,7.41;N,17.59 Specific rotation $[\alpha]_D^{20}$-27.9° (c=0.1,DMSO)
201		colorless crystals NMR(DMSO-d_6) δ ppm:1.62(2H,br-s),2.80(1H,dd,J=14,5Hz),2.85(1H,dd,J=14,4.5Hz),2.98(4H,t,J=5Hz),3.82(1H,dd,J=9,6.5Hz),3.90(4H,t,J=5Hz),4.02(1H,t,J=9Hz),4.55-4.65(1H,m),7.08(1H,t,J=9Hz),7.20(1H,dd,J=9,2.5Hz),7.39(2H,br-s),7.50(1H,dd,J=15,2.5Hz) IR ν (KBr) cm^{-1}:1714,3384 Specific rotation $[\alpha]_D^{20}$-37.0° (c=0.1,DMSO)
202		colorless crystals [DMF-H_2O] mp,167.5～169.5℃ Elemental analysis for $C_{16}H_{22}FN_5O_2S$ Calcd. % : C,52.30;H,6.03;N,19.06 Found % : C,52.13;H,5.99;N,19.08 Specific rotation $[\alpha]_D^{20}$-47.0° (c=0.1,DMSO)

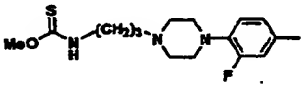
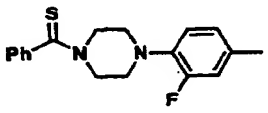


Reference example	R	Physical properties [recrystallization solvent]
203		colorless needles [CH_3CN] mp,172.5～174℃ Elemental analysis for $C_{17}H_{24}FN_5O_2S$ Calcd. % : C,53.53;H,6.34;N,18.36 Found % : C,53.37;H,6.16;N,18.11 Specific rotation $[\alpha]_D^{20}$-32.0° (c=0.1,DMSO)
204		colorless crystals [MeOH] mp,171～173℃ Elemental analysis for $C_{18}H_{26}FN_5O_2S$ Calcd. % : C,54.66;H,6.63;N,17.71 Found % : C,54.53;H,6.45;N,17.37 Specific rotation $[\alpha]_D^{20}$-34.9° (c=0.1,DMSO)
205		colorless prisms [MeOH] mp,178～179.5℃ Elemental analysis for $C_{17}H_{24}FN_5O_2S$ Calcd. % : C,53.53;H,6.34;N,18.36 Found % : C,53.54;H,6.25;N,18.19 Specific rotation $[\alpha]_D^{20}$-31.0° (c=0.1,DMSO)
206		pale brown crystals NMR(DMSO-d_6) δ ppm:1.70(2H,br-s),2.80(1H,dd,J=13.5,5Hz),2.85(1H,dd,J=13.5,5Hz),2.95-3.10(4H,m),3.81(1H,dd,J=9,6.5Hz),3.81-3.90(2H,m),3.98(3H,s),4.02(1H,t,J=9Hz),4.10-4.20(2H,m),4.55-4.65(1H,m),7.08(1H,t,J=9Hz),7.21(1H,dd,J=9,2.5Hz),7.50(1H,dd,J=14.5,2.5Hz) IR ν (KBr) cm^{-1}:1730,3388 MS(m/z):368(M^+) Specific rotation $[\alpha]_D^{20}$-29.1° (c=0.1,DMSO)
207	 · HCl	pale brown scales [H_2O] mp,240～243.5℃ Elemental analysis for $C_{17}H_{23}FN_4O_3S \cdot HCl$ Calcd. % : C,48.74;H,5.77;N,13.37 Found % : C,48.57;H,5.53;N,13.27 Specific rotation $[\alpha]_D^{20}$-39.8° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
208		brown crystals NMR(DMSO-d6) δ ppm:0.94(3H,t,J=7Hz),1.67(2H,br-s),1.71(2H,sex,J=7Hz),2.79(1H,dd,J=13.5,5Hz),2.85(1H,dd,J=13.5,5Hz),2.90-3.10(4H,m),3.75-3.90(3H,m),4.02(1H,t,J=9Hz),4.10-4.20(2H,m),4.38(2H,t,J=7Hz),4.55-4.65(1H,m),7.08(1H,t,J=9Hz),7.20(1H,d,J=9Hz),7.50(1H,dd,J=14.5,2Hz) IR ν (KBr) cm^{-1}:1738,3380 MS(m/z):396(M$^+$) Specific rotation [α]$_D^{20}$-28.9° (c=0.1,DMSO)
209		grayish brown crystals NMR(DMSO-d6) δ ppm:2.61(3H,s),3.11(4H,t,J=5Hz),3.15-3.25(2H,m),3.86(1H,dd,J=9,6.5Hz),4.15(1H,t,J=9Hz),4.20-4.40(4H,m),4.85-4.95(1H,m),7.12(1H,t,J=9Hz),7.19(1H,dd,J=9,2.5Hz),7.49(1H,dd,J=14.5,2.5Hz),7.98(2H,br-s) IR ν (KBr) cm^{-1}:1754,3464 MS(m/z):384(M$^+$) Specific rotation [α]$_D^{20}$-36.8° (c=0.1,DMSO)
210		pale brown liquid NMR(DMSO-d6) δ ppm:1.68(2H,quin,J=7Hz),2.37(2H,t,J=7Hz),2.53(4H,t,J=4.5Hz),2.80-2.90(2H,m),2.83(3H,d,J=4.5Hz),3.00(4H,t,J=4.5Hz),3.38(2H,br-s),3.81(1H,dd,J=9,6.5Hz),4.03(1H,t,J=9Hz),4.55-4.65(1H,m),7.04(1H,t,J=9Hz),7.18(1H,dd,J=9,2.5Hz),7.32(1H,br-s),7.39(1H,br-s),7.47(1H,dd,J=15.5,2.5Hz) IR ν (liq.) cm^{-1}:1740,3308 Specific rotation [α]$_D^{20}$-21.0° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
211		brown amorphous solid NMR(DMSO-d_6) δ ppm:1.55-1.80(4H,m),2.38(2H,t,J=6.5Hz),2.53(4H,t,J=5Hz),2.83(1H,dd,J=13.5,5Hz),2.87(1H,dd,J=13.5,5Hz),3.01(4H,t,J=5Hz),3.40-3.50(2H,m),3.79(1H,dd,J=9,6.5Hz),3.87(3H,s),4.01(1H,t,J=9Hz),4.50-4.60(1H,m),7.02(1H,t,J=9Hz),7.17(1H,dd,J=9,2.5Hz),7.42(1H,dd,J=15.5,2.5Hz),8.77(1H,br-s) IR ν (liq.) cm^{-1}:1746,3284 MS(m/z):425(M^+) Specific rotation $[\alpha]_D^{20}$-28.4° (c=0.1,DMSO)
212		yellow crystals[$ClCH_2CH_2Cl$-AcOEt] mp,183~186°C Elemental analysis for $C_{21}H_{23}FN_4O_2S \cdot 1/4H_2O$ Calcd. % : C,60.20;H,5.65;N,13.37 Found % : C,60.28;H,5.50;N,13.14 Specific rotation $[\alpha]_D^{20}$-26.9° (c=0.1,DMSO)

Reference example 213

[0129] (S)-5-Aminomethyl-3-[4-(4-aminopiperidin-1-yl)-3-fluorophenyl]-2-oxooxazoli dine dihydrochloride

[0130] A suspension of 4.70 g of (S)-5-azidomethyl-3-[3-fluoro-4-(4-hydroxyiminopiperidin-1-yl)phenyl]-2-oxooxazolidine and 4.70 ml of Raney nickel in 95 ml of 10 % ammonia methanol solution was stirred at 40°C at a hydrogen pressure of under 30 atm for 6 hours. The catalyst was filtered off, and the filtrate was concentrated under reduced pressure. The residue was added with ethanol and 33% hydrogen chloride ethanol solution, and the mixture was stirred under ice-cooling for 1 hour. The precipitated crystals were collected by filtration to obtain 5.66 g of pale brown crystals.
NMR spectrum (DMSO-d_6) δ ppm:
1.65-1.80(2H,m),2.00-2.10(2H,m),2.70-2.80(2H,m),3.10-3.25(3H,m),3.30-3.40(2H,m), 3.89(1H,dd,J=9,6.5Hz),4.15(1H,t,J=9Hz),4.90-5.00(1H,m),7.10(1H,t,J=9Hz), 7.17(1H,dd,J=9,2.5Hz),7.45(1H,dd,J=14.5,2.5Hz),8.29(3H,br-s),8.47(3H,br-s)
IR spectrum v (KBr) cm^{-1}: 1744,3440
Specific rotation $[\alpha]_D^{20}$ -33.8° (c = 0.1, DMSO)

Reference example 214

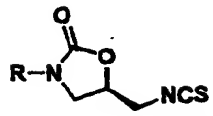
[0131] (R)-N-[2-Oxo-3-[4-(thiomorpholin-4-yl)phenyl]oxazolidin-5-yl]methyl isothiocyanate

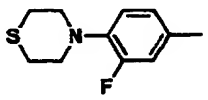
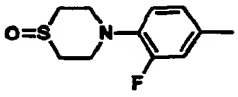
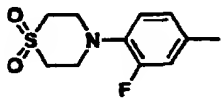
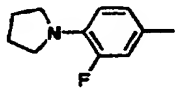
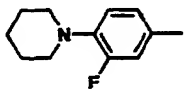
[0132] To a mixture of 1.0 g of (S)-5-aminomethyl-2-oxo-3-[4-(thiomorpholin-4-yl)-phenyl]oxazolidine in 10 ml of benzene and 1 ml of N,N-dimethylformamide, 0.50 ml of triethylamine and 0.20 ml of carbon disulfide were added, and the mixture was stirred at room temperature for 6 hours. The reaction solution was concentrated under reduced pressure, and the residue was added with 10 ml of dichloromethane and 0.50 ml of triethylamine. The mixture was added with 0.35 ml of ethyl chlorocarbonate under ice-cooling and with stirring, and stirred at the same temperature for 30 minutes. The reaction solution was added with water, and the precipitated crystals were collected by filtration to obtain 0.98 g of colorless crystals. Recrystallization from a mixture of N,N-dimethylformamide-water gave colorless crystals having the melting point of from 194.5 to 195.5°C.

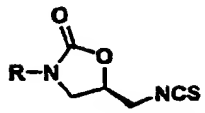
Elemental analysis for $C_{15}H_{17}N_3O_2S_2$						
Calculated %	C,	53.71;	H,	5.11;	N,	12.53
Found %	C,	53.53;	H,	5.07;	N,	12.54

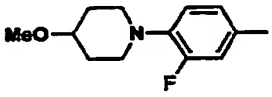
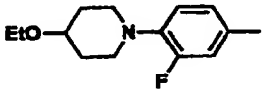
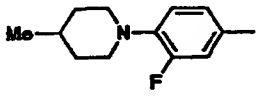
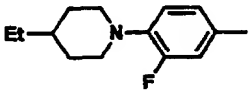
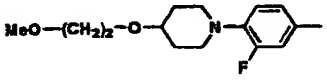
Specific rotation $[\alpha]_D^{20}$ -151.8° (c =0.1, DMSO)

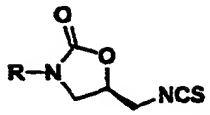
[0133] The compounds of Reference examples 215 through 264 were obtained in the same manner as in Reference example 214.

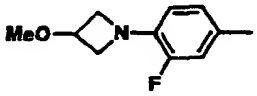
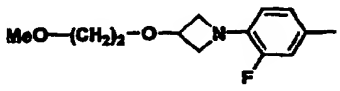
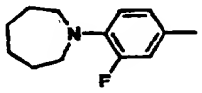
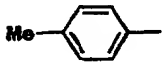
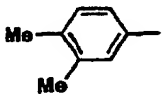


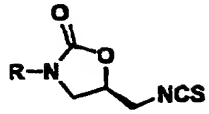
Reference example	R	Physical properties [recrystallization solvent]
215		pale yellow columns [CH_3CN] mp,135.5～136.5℃ Elemental analysis for $C_{15}H_{16}FN_3O_2S_2$ Calcd. % : C,50.97;H,4.56;N,11.89 Found % : C,51.01;H,4.60;N,11.85 Specific rotation $[\alpha]_D^{20}$-151.9° (c=0.1,DMSO)
216		colorless amorphous solid NMR($CDCl_3$) δ ppm:2.95-3.10(4H,m),3.25-3.30(2H,m),3.75-3.85(2H,m),3.85-3.95(2H,m),3.97(1H,dd,J=14.5,5.5Hz),4.17(1H,t,J=9Hz),4.80-4.90(1H,m),7.05-7.15(2H,m),7.52(1H,d,J=13.5Hz) IR ν (KBr) cm^{-1}:1754,2096 MS(m/z):369(M^+) Specific rotation $[\alpha]_D^{20}$-94.4° (c=0.1,DMSO)
217		yellow liquid NMR(DMSO-d_6) δ ppm:3.23(4H,t,J=5Hz),3.49(4H,t,J=5Hz),3.80(1H,dd,J=9,5.5Hz),4.02(1H,dd,J=15.5,5.5Hz),4.10(1H,dd,J=15.5,3.5Hz),4.19(1H,t,J=9Hz),4.90-5.00(1H,m),7.15-7.25(2H,m),7.50(1H,dd,J=15,2Hz) IR ν (liq.) cm^{-1}:1754,2100 MS(m/z):385(M^+) Specific rotation $[\alpha]_D^{20}$-123.3° (c=0.1,DMSO)
218		pale yellow crystals [i-PrOH] mp,109.5～110℃ Elemental analysis for $C_{15}H_{16}FN_3O_2S$ Calcd. % : C,56.06;H,5.02;N,13.08 Found % : C,56.09;H,5.32;N,13.12 Specific rotation $[\alpha]_D^{20}$-166.3° (c=0.1,DMSO)
219		pale brown crystals [i-PrOH] mp,107～109℃ Elemental analysis for $C_{16}H_{18}FN_3O_2S$ Calcd. % : C,57.30;H,5.41;N,12.53 Found % : C,57.25;H,5.63;N,12.52 Specific rotation $[\alpha]_D^{20}$-154.2° (c=0.1,DMSO)

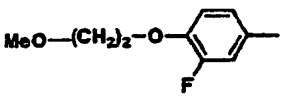
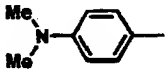
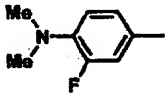
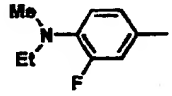
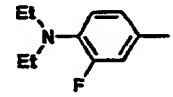


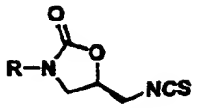
Reference example	R	Physical properties [recrystallization solvent]
220		colorless prisms[AcOEt-i-Pr_2O] mp,118.5～120℃ Elemental analysis for $C_{17}H_{20}FN_3O_3S$ Calcd. % : C,55.88;H,5.52;N,11.50 Found % : C,55.89;H,5.58;N,11.41 Specific rotation $[\alpha]_D^{20}$-146.6° (c=0.1,DMSO)
221		colorless crystals[i-PrOH] mp,114.5～116℃ Elemental analysis for $C_{18}H_{22}FN_3O_3S$ Calcd. % : C,56.98;H,5.84;N,11.07 Found % : C,56.97;H,5.88;N,10.93 Specific rotation $[\alpha]_D^{20}$-136.4° (c=0.1,DMSO)
222		colorless needles[AcOEt-i-Pr_2O] mp,133.5～134.5℃ Elemental analysis for $C_{17}H_{20}FN_3O_2S$ Calcd. % : C,58.43;H,5.77;N,12.03 Found % : C,58.39;H,5.67;N,11.95 Specific rotation $[\alpha]_D^{20}$-153.5° (c=0.1,DMSO)
223		colorless needles[Toluene] mp,94～95℃ Elemental analysis for $C_{18}H_{22}FN_3O_2S$ Calcd. % : C,59.48;H,6.10;N,11.56 Found % : C,59.27;H,6.12;N,11.43 Specific rotation $[\alpha]_D^{20}$-147.9° (c=0.1,DMSO)
224		colorless crystals[AcOEt-i-Pr_2O] mp,63～64℃ Elemental analysis for $C_{19}H_{24}FN_3O_4S$ Calcd. % : C,55.73;H,5.91;N,10.26 Found % : C,55.64;H,5.99;N,10.27 Specific rotation $[\alpha]_D^{20}$-130.7° (c=0.1,DMSO)

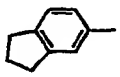
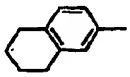
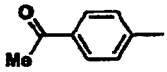
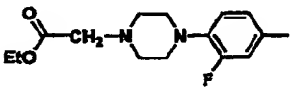
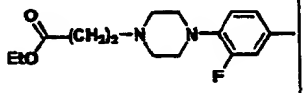
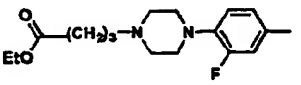


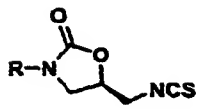
Reference example	R	Physical properties [recrystallization solvent]
225		brown liquid NMR(DMSO-d_6) δ ppm:3.24(3H,s),3.60-3.70(2H,m),3.75(1H,dd,J=9,5.5Hz),3.95-4.20(5H,m),4.25-4.35(1H,m),4.85-4.95(1H,m),6.59(1H,dd,J=10.5,8.5Hz),7.12(1H,dd,J=8.5,2Hz),7.36(1H,dd,J=14.5,2Hz) IR ν (liq.) cm^{-1}:1754,2100 MS(m/z):337(M^+) Specific rotation $[\alpha]_D^{20}$-129.3° (c=0.1,DMSO)
226		colorless needles[AcOEt-i-Pr_2O] mp,78.5～79.5℃ Elemental analysis for $C_{17}H_{20}FN_3O_4S$ Calcd. % : C,53.53;H,5.29;N,11.02 Found % : C,53.47;H,5.47;N,10.93 Specific rotation $[\alpha]_D^{20}$-140.4° (c=0.1,DMSO)
227		colorless crystals[AcOEt-i-Pr_2O] mp,128～129℃ Elemental analysis for $C_{17}H_{20}FN_3O_2S$ Calcd. % : C,58.43;H,5.77;N,12.03 Found % : C,58.50;H,5.97;N,11.95 Specific rotation $[\alpha]_D^{20}$-153.8° (c=0.1,DMSO)
228		pale brown liquid NMR(DMSO-d_6) δ ppm:2.28(3H,s),3.79(1H,dd,J=9,5.5Hz),4.04(1H,dd,J=15,5Hz),4.10(1H,dd,J=15,3Hz),4.19(1H,t,J=9Hz),4.90-4.96(1H,m),7.20(2H,d,J=8.5Hz),7.43(2H,d,J=8.5Hz) IR ν (liq.) cm^{-1}:1756,2096 MS(m/z):248(M^+) Specific rotation $[\alpha]_D^{20}$-178.3° (c=0.1,DMSO)
229		colorless prisms[i-PrOH] mp,92～92.5℃ Elemental analysis for $C_{13}H_{14}N_2O_2S$ Calcd. % : C,59.52;H,5.38;N,10.68 Found % : C,59.54;H,5.39;N,10.65 Specific rotation $[\alpha]_D^{20}$-175.1° (c=0.1,DMSO)

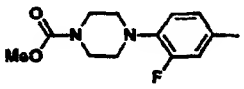
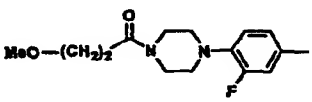
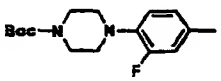
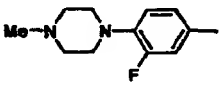
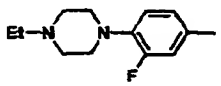
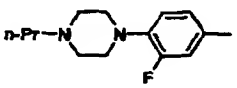


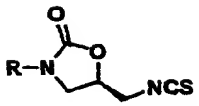
Reference example	R	Physical properties [recrystallization solvent]
230		pale brown crystals [AcOEt] mp,71.5～73.5℃ Elemental analysis for $C_{14}H_{15}FN_2O_4S$ Calcd. % : C,51.53;H,4.63;N,8.58 Found % : C,51.46;H,4.56;N,8.49 Specific rotation $[\alpha]_D^{20}$-137.7° (c=0.1,DMSO)
231		colorless needles[AcOEt-i-Pr_2O] mp,140.5～141.5℃ Elemental analysis for $C_{13}H_{15}N_3O_2S$ Calcd. % : C,56.30;H,5.45;N,15.15 Found % : C,56.45;H,5.35;N,14.95 Specific rotation $[\alpha]_D^{20}$-172.5° (c=0.1,DMSO)
232		pale yellow needles[i-PrOH] mp,74.5～75℃ Elemental analysis for $C_{13}H_{14}FN_3O_2S$ Calcd. % : C,52.87;H,4.78;N,14.23 Found % : C,52.81;H,4.99;N,14.18 Specific rotation $[\alpha]_D^{20}$-172.7° (c=0.1,DMSO)
233		colorless needles[AcOEt-i-Pr_2O] mp,78～79℃ Elemental analysis for $C_{14}H_{16}FN_3O_2S$ Calcd. % : C,54.35;H,5.21;N,13.58 Found % : C,54.42;H,5.30;N,13.63 Specific rotation $[\alpha]_D^{20}$-177.5° (c=0.1,DMSO)
234		pale brown liquid NMR(DMSO-d_6) δ ppm:1.00(6H,t,J=7.5Hz), 3.13(4H,q,J=7.5Hz),3.78(1H,dd,J=9.5,6Hz),4.03(1H,dd,J=15.5,5.5Hz),4.11(1H,dd,J=15.5,3.5Hz),4.17(1H,t,J=9.5Hz),4.90-5.00(1H,m),7.04(1H,t,J=9Hz),7.17(1H,dd,J=9,2.5Hz),7.41(1H,dd,J=14.5,2.5Hz) MS(m/z):323(M^+) Specific rotation $[\alpha]_D^{20}$-162.3° (c=0.1,DMSO)

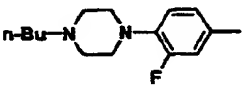
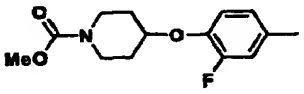
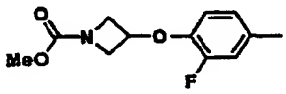
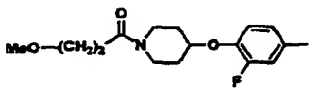


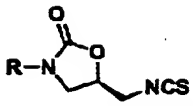
Reference example	R	Physical properties [recrystallization solvent]
235		colorless needles[AcOEt] mp,103.5～104.5℃ Elemental analysis for $C_{14}H_{14}N_2O_2S$ Calcd. % : C,61.29;H,5.14;N,10.21 Found % : C,61.24;H,5.13;N,10.20 Specific rotation $[\alpha]_D^{20}$-172.7° (c=0.1,DMSO)
236		colorless needles[i-PrOH] mp,122.5～124℃ Elemental analysis for $C_{15}H_{16}N_2O_2S$ Calcd. % : C,62.48;H,5.59;N,9.71 Found % : C,62.49;H,5.61;N,9.65 Specific rotation $[\alpha]_D^{20}$-166.8° (c=0.1,DMSO)
237		pale yellow crystals NMR(DMSO-d6) δ ppm:2.55(3H,s),3.89(1H,dd,J=9.5,5.5Hz),4.08(1H,dd,J=15,5.5Hz),4.15(1H,dd,J=15,3.5Hz),4.28(1H,t,J=9.5Hz),4.98-5.03(1H,m),7.70(2H,d,J=9Hz),8.00(2H,d,J=9Hz) IR ν (KBr) cm^{-1}:1748,2092 MS(m/z):276(M^+) Specific rotation $[\alpha]_D^{20}$-195.6° (c=0.1,DMSO)
238		pale brown needles[AcOEt-i-Pr_2O] mp,117～119℃ Elemental analysis for $C_{19}H_{23}FN_4O_4S$ Calcd. % : C,54.02;H,5.49;N,13.26 Found % : C,54.30;H,5.40;N,13.00 Specific rotation $[\alpha]_D^{20}$-103.2° (c=0.1,DMSO)
239		pale yellow needles[i-PrOH] mp,92.5～94℃ Elemental analysis for $C_{20}H_{25}FN_4O_4S$ Calcd. % : C,55.03;H,5.77;N,12.84 Found % : C,54.84;H,5.87;N,12.71 Specific rotation $[\alpha]_D^{20}$-121.8° (c=0.1,DMSO)
240		colorless needles[AcOEt-i-Pr_2O] mp,95.5～97℃ Elemental analysis for $C_{21}H_{27}FN_4O_4S$ Calcd. % : C,55.98;H,6.04;N,12.44 Found % : C,55.70;H,5.76;N,12.29 Specific rotation $[\alpha]_D^{20}$-108.3° (c=0.1,DMSO)

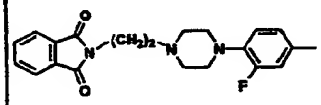
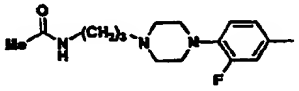
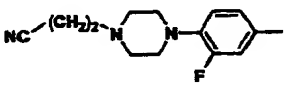
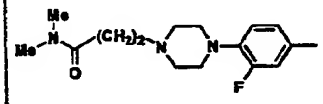


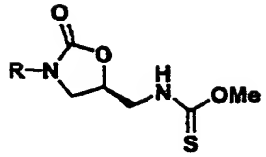
Reference example	R	Physical properties [recrystallization solvent]
241		colorless crystals [i-PrOH] mp,102～103℃ Elemental analysis for $C_{17}H_{19}FN_4O_4S$ Calcd. % : C,51.77;H,4.86;N,14.20 Found % : C,51.77;H,4.83;N,14.10 Specific rotation [α]$_D^{20}$-139.5° (c=0.1,DMSO)
242		pale yellow crystals[MeOH] mp,110～112℃ Elemental analysis for $C_{19}H_{23}FN_4O_4S \cdot 1/4H_2O$ Calcd. % : C,53.45;H,5.55;N,13.12 Found % : C,53.60;H,5.46;N,13.04 Specific rotation [α]$_D^{20}$-123.9° (c=0.1,DMSO)
243		colorless needles [AcOEt-i-Pr_2O] mp,142～143.5℃ Elemental analysis for $C_{20}H_{25}FN_4O_4S$ Calcd. % : C,55.03;H,5.77;N,12.84 Found % : C,54.96;H,5.88;N,12.79 Specific rotation [α]$_D^{20}$-121.1° (c=0.1,DMSO)
244		colorless prisms [THF-i-Pr_2O] mp,127～127.5℃ Elemental analysis for $C_{16}H_{19}FN_4O_2S$ Calcd. % : C,54.84;H,5.47;N,15.99 Found % : C,54.83;H,5.41;N,15.84 Specific rotation [α]$_D^{20}$-159.0° (c=0.1,DMSO)
245		colorless needles [AcOEt-i-Pr_2O] mp,86.5～87.5℃ Elemental analysis for $C_{17}H_{21}FN_4O_2S$ Calcd. % : C,56.03;H,5.81;N,15.37 Found % : C,56.09;H,5.76;N,15.46 Specific rotation [α]$_D^{20}$-151.2° (c=0.1,DMSO)
246		colorless crystals [AcOEt-i-Pr_2O] mp,93～94℃ Elemental analysis for $C_{18}H_{23}FN_4O_2S$ Calcd. % : C,57.12;H,6.13;N,14.80 Found % : C,57.02;H,6.13;N,14.75 Specific rotation [α]$_D^{20}$-141.6° (c=0.1,DMSO)

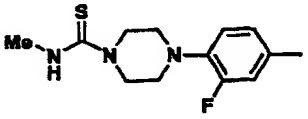
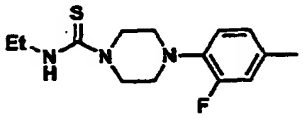
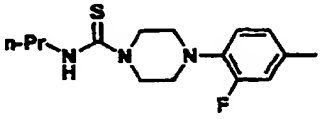
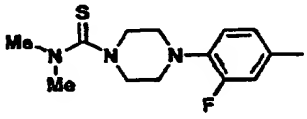
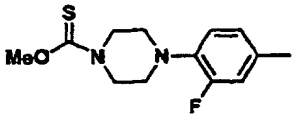


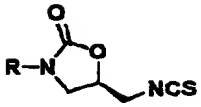
Reference example	R	Physical properties [recrystallization solvent]
247		pale yellow plates[i-PrOH] mp,101～102℃ Elemental analysis for $C_{19}H_{25}FN_4O_2S$ Calcd. % : C,58.14;H,6.42;N,14.27 Found % : C,58.06;H,6.51;N,14.16 Specific rotation $[\alpha]_D^{20}$-133.8° (c=0.1,DMSO)
248		yellowish brown liquid NMR(DMSO-d_6) δ ppm:1.50-1.70(2H,m),1.85-1.95(2H,m),3.20-3.30(2H,m),3.60(3H,s),3.60-3.70(2H,m),3.79(1H,dd,J=9,6Hz),4.02(1H,dd,J=15.5,5.5Hz),4.11(1H,dd,J=15.5,3.5Hz),4.19(1H,t,J=9Hz),4.45-4.55(1H,m),4.90-5.00(1H,m),7.22(1H,dd,J=9,2.5Hz),7.26(1H,t,J=9Hz),7.52(1H,dd,J=13.5,2.5Hz) IR ν (liq.) cm^{-1}:1696,1758,2096 MS(m/z):409(M^+) Specific rotation $[\alpha]_D^{20}$-108.0° (c=0.1,DMSO)
249		colorless prisms[AcOEt] mp,121～122℃ Elemental analysis for $C_{16}H_{16}FN_3O_5S$ Calcd. % : C,50.39;H,4.23;N,11.02 Found % : C,50.29;H,4.20;N,10.87 Specific rotation $[\alpha]_D^{20}$-133.1° (c=0.1,DMSO)
250		colorless amorphous solid NMR(DMSO-d_6) δ ppm:1.50-1.70(2H,m),1.80-2.00(2H,m),2.57(2H,t,J=6.5Hz),3.20-3.40(2H,m),3.23(3H,s),3.56(2H,t,J=6.5Hz),3.65-3.75(1H,m),3.80(2H,dd,J=9,6Hz),4.03(1H,dd,J=15,5.5Hz),4.10(1H,dd,J=15,3Hz),4.19(1H,t,J=9Hz),4.50-4.60(1H,m),4.90-5.00(1H,m),7.22(1H,dd,J=9,2.5Hz),7.27(1H,t,J=9Hz),7.52(1H,dd,J=13.5,2.5Hz) IR ν (KBr) cm^{-1}:1756,2120 MS(m/z):437(M^+) Specific rotation $[\alpha]_D^{20}$-113.5° (c=0.1,DMSO)

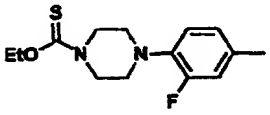
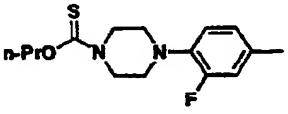
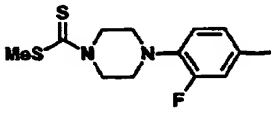
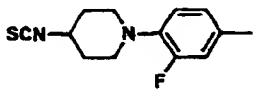


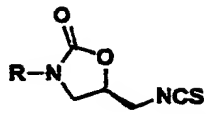
Reference example	R	Physical properties [recrystallization solvent]
251		yellow crystals [DMF-H_2O] mp,209~211℃ Elemental analysis for $C_{25}H_{24}FN_5O_4S$ Calcd. % : C,58.93;H,4.75;N,13.74 Found % : C,58.85;H,4.68;N,13.65 Specific rotation $[\alpha]_D^{20}$-117.9° (c=0.1,DMSO)
252		pale brown liquid NMR(DMSO-d_6) δ ppm:1.55-1.65(2H,m),1.79(3H,s),2.30-2.40(2H,m),2.40-2.50(4H,m),2.90-3.00(4H,m),3.00-3.10(2H,m),3.45-3.55(2H,m),3.79(1H,dd,J=9,6.5Hz),4.13(1H,t,J=9Hz),4.85-4.95(1H,m),7.04(1H,t,J=9Hz),7.18(1H,dd,J=9,2.5Hz),7.47(1H,dd,J=14.5,2.5Hz),7.70(1H,br-s) IR ν (liq.) cm^{-1}:1746 Specific rotation $[\alpha]_D^{20}$-66.8° (c=0.1,DMSO)
253		colorless crystals [AcOEt] mp,103.5~105.5℃ Elemental analysis for $C_{18}H_{20}FN_5O_2S$ Calcd. % : C,55.51;H,5.18;N,17.98 Found % : C,55.45;H,5.11;N,17.89 Specific rotation $[\alpha]_D^{20}$-146.3° (c=0.1,DMSO)
254		pale brown crystals NMR(DMSO-d_6) δ ppm:2.50-2.70(4H,m),2.82(3H,s),2.90-3.10(4H,m),2.98(3H,s),3.78(1H,dd,J=9.5,6Hz),4.02(1H,dd,J=15,5Hz),4.10(1H,dd,J=15,3.5Hz),4.17(1H,t,J=9.5Hz),4.90-5.00(1H,m),7.05(1H,t,J=9Hz),7.19(1H,dd,J=9,2.5Hz),7.45(1H,dd,J=15,2.5Hz) IR ν (KBr) cm^{-1}:1630,1762,2132 MS(m/z):435(M^+) Specific rotation $[\alpha]_D^{20}$-108.1° (c=0.1,DMSO)

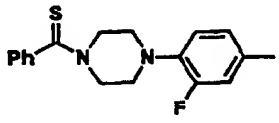


Reference example	R	Physical properties [recrystallization solvent]
255		pale brown crystals [CH_3CN] mp,174~175.5℃ Elemental analysis for $C_{17}H_{20}FN_5O_2S_2$ Calcd. % : C,49.86;H,4.92;N,17.10 Found % : C,49.97;H,4.81;N,16.94 Specific rotation $[\alpha]_D^{20}$-125.7° (c=0.1,DMSO)
256		pale brown crystals [CH_3CN] mp,233~235℃ Elemental analysis for $C_{18}H_{22}FN_5O_2S_2$ Calcd. % : C,51.05;H,5.24;N,16.54 Found % : C,51.08;H,5.18;N,16.36 Specific rotation $[\alpha]_D^{20}$-121.8° (c=0.1,DMSO)
257		colorless crystals [$ClCH_2CH_2Cl$] mp,183.5~185.5℃ Elemental analysis for $C_{19}H_{24}FN_5O_2S_2 \cdot 1/2H_2O$ Calcd. % : C,51.10;H,5.64;N,15.68 Found % : C,51.24;H,5.48;N,15.42 Specific rotation $[\alpha]_D^{20}$-118.1° (c=0.1,DMSO)
258		colorless crystals [CH_3CN] mp,197~198.5℃ Elemental analysis for $C_{18}H_{22}FN_5O_2S_2$ Calcd. % : C,51.05;H,5.24;N,16.54 Found % : C,51.23;H,5.19;N,16.65 Specific rotation $[\alpha]_D^{20}$-119.3° (c=0.1,DMSO)
259		colorless crystals [AcOEt] mp,132~133℃ Elemental analysis for $C_{17}H_{19}FN_4O_3S_2$ Calcd. % : C,49.74;H,4.67;N,13.65 Found % : C,49.87;H,4.74;N,13.44 Specific rotation $[\alpha]_D^{20}$-115.6° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
260		pale yellow crystals NMR(DMSO-d_6) δ ppm:1.30(3H,t,J=6.5Hz),3.00-3.10(4H,m),3.79(1H,dd,J=9,6Hz),3.82-3.88(2H,m),4.02(1H,dd,J=15,5Hz),4.12(1H,dd,J=15,4Hz),4.10-4.15(2H,m),4.18(1H,t,J=9Hz),4.47(2H,q,J=6.5Hz),4.90-5.00(1H,m),7.10(1H,t,J=9Hz),7.21(1H,d,J=9Hz),7.50(1H,d,J=14.5Hz) IR ν (KBr) cm^{-1}:1748,2228 MS(m/z):424(M^+) Specific rotation $[\alpha]_D^{20}$-131.4° (c=0.1,DMSO)
261		pale brown crystals[AcOEt] mp,156~158℃ Elemental analysis for $C_{19}H_{23}FN_4O_3S_2$ Calcd. % : C,52.04;H,5.29;N,12.78 Found % : C,52.32;H,5.29;N,12.70 Specific rotation $[\alpha]_D^{20}$-121.6° (c=0.1,DMSO)
262		pale brown crystals[AcOEt-i-Pr_2O] mp,138~140℃ Elemental analysis for $C_{17}H_{19}FN_4O_2S_3$ Calcd. % : C,47.87;H,4.49;N,13.13 Found % : C,47.75;H,4.59;N,12.84 Specific rotation $[\alpha]_D^{20}$-110.4° (c=0.1,DMSO)
263		pale brown crystals[AcOEt-i-Pr_2O] mp,113~115℃ Elemental analysis for $C_{17}H_{17}FN_4O_2S_2$ Calcd. % : C,52.02;H,4.37;N,14.28 Found % : C,51.82;H,4.46;N,14.00 Specific rotation $[\alpha]_D^{20}$-125.4° (c=0.1,DMSO)



Reference example	R	Physical properties [recrystallization solvent]
264		yellow amorphous solid NMR($CDCl_3$) δ ppm:3.04(2H,t,J=5Hz),3.27(2H,t,J=5Hz),3.76(2H,t,J=5Hz),3.80-3.90(2H,m),3.96(1H,dd,J=15,5Hz),4.15(1H,t,J=9Hz),4.60(2H,t,J=5Hz),4.80-4.85(1H,m),6.95(1H,t,J=9Hz),7.13(1H,dd,J=9,2.5Hz),7.30-7.40(5H,m),7.46(1H,dd,J=14,2.5Hz) IR ν (KBr) cm^{-1}:1754,2080 Specific rotation $[\alpha]_D^{20}$-106.6° (c=0.1,DMSO)

Reference example 265

[0134] (R)-1-[4-[2-Fluoro-4-(5-isothiocyanatomethyl-2-oxooxazolidin-3-yl)phenyl]-piperazine]carbothioamide

[0135] To a solution of 0.79 g of 1,1'-thiocarbonyl diimidazole and 0.52 ml of triethylamine in 20 ml of 1,2-dichloroethane, 1.20 g of (R)-1-[4-[4-(5-aminomethyl-2-oxooxazolidin-3-yl)-2-fluorophenyl]piperazine]carbothioamide was added under ice-cooling, and the mixture was stirred at room temperature for 18 hours. The reaction solution was added with water and 1,2-dichloroethane, and the insoluble solid was removed. Then, the 1,2-dichloroethane layer was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, 1,2-dichloroethane : methanol = 20 : 1) to obtain 0.25 g of yellow crystals.

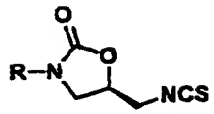
NMR spectrum (DMSO-d_6) δ ppm:

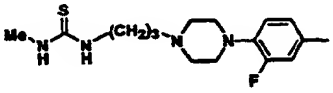
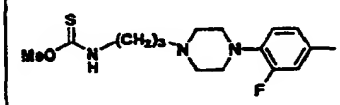
2.99(4H,t,J=5Hz),3.79(1H,dd,J=9.5,5.5Hz),3.90(4H,t,J=5Hz),4.02(1H,dd,J=15,5.5Hz), 4.10(1H,dd,J=15,4Hz),4.18(1H,t,J=9Hz),4.90-5.00(1H,m),7.09(1H,t,J=9Hz), 7.20(1H,dd,J=9,2.5Hz),7.39(2H,br-s),7.48(1H,dd,J=14.5,2.5Hz)

IR spectrum ν (KBr) cm^{-1}: 1746,2220

Specific rotation $[\alpha]_D^{20}$ -130.4° (c = 0.1, DMSO)

[0136] The compounds of Reference examples 266 through 267 were obtained in the same manner as in Reference example 265.



Reference example	R	Physical properties [recrystallization solvent]
266		pale yellow crystals NMR(DMSO-d6) δ ppm:1.69(2H,quin,J=7 Hz),2.42(2H,t,J=7Hz),2.58(4H,s),2.82(3H,d,J=4.5Hz),3.02(4H,s),3.35-3.45(2 H,m),3.78(1H,dd,J=9,6Hz),4.02(1H,dd ,J=15,5Hz),4.11(1H,dd,J=15,3.5Hz),4. 18(1H,t,J=9Hz),4.90-5.00(1H,m),7.06(1H,t,J=9Hz),7.19(1H,dd,J=9,2.5Hz),7. 32(1H,br-s),7.39(1H,br-s),7.46(1H,dd, J=14.5,2.5Hz) IR ν (KBr) cm-1:1744,2088,3280 Specific rotation [α]D20-44.0° (c=0.1,DMSO)
267		orange liquid NMR(DMSO-d6) δ ppm:1.60-1.80(2H,m), 2.39(2H,t,J=6.5Hz),2.53(4H,t,J=5Hz), 3.02(4H,t,J=5Hz),3.40-3.50(2H,m),3.7 7(1H,dd,J=9,6Hz),3.87(3H,s),3.99(1H, dd,J=15,5Hz),4.07(1H,dd,J=15,3.5Hz), 4.17(1H,t,J=9Hz),4.85-4.95(1H,m),7.0 3(1H,t,J=9Hz),7.17(1H,dd,J=9,2.5Hz), 7.41(1H,dd,J=15.5,2.5Hz),8.77(1H,br-s) IR ν (liq.) cm-1:1752,2088,3296 Specific rotation [α]D20-67.5° (c=0.1,DMSO)

Example 1

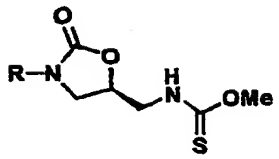
[0137] O-Methyl (S)-N-[3-[3-fluoro-4-(thiomorpholin-4-yl)phenyl]-2-oxooxazolidin-5-yl]methylthiocarbamate

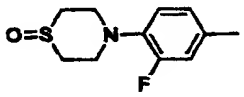
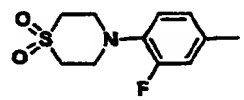
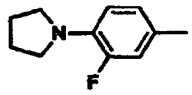
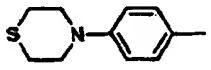
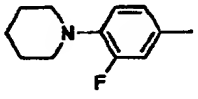
[0138] To 44 ml of dried methanol, 0.53 g of 60 % sodium hydride was added under ice-cooling and with stirring, and the mixture was stirred at room temperature for 30 minutes. Then, the mixture was added with 4.41 g of (R)-N-[3-[3-fluoro-4-(thiomorpholin-4-yl)phenyl]-2-oxooxazolidin-5-yl]methyl isothiocyanate, and stirred at room temperature for 3 hours. The reaction mixture was neutralized with ice water and 10% hydrochloric acid, and the precipitated crystals were collected by filtration to obtain 4.68 g of pale brown crystals. Recrystallization from ethanol gave pale brown crystals having the melting point of from 141.5 to 143°C.

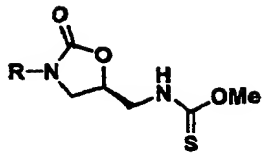
Elemental analysis for $C_{16}H_{20}FN_3O_3S_2$						
Calculated %	C,	49.85;	H,	5.23;	N,	10.90
Found %	C,	49.58;	H,	5.05;	N,	10.82

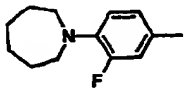
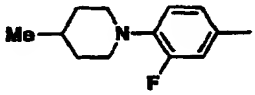
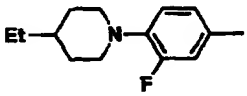
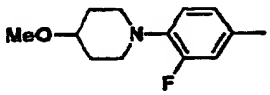
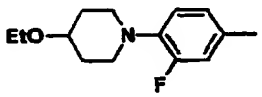
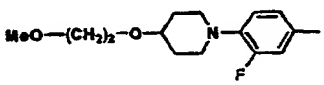
Speck rotation $[\alpha]_D^{20}$ -25.9° (c =0.1, DMSO)

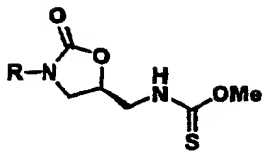
[0139] The compounds of Examples 2 through 60 were obtained in the same manner as in Example 1.

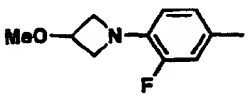
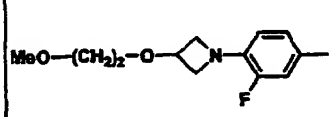
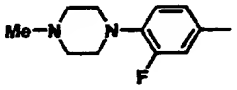
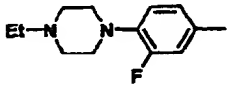
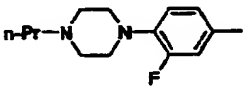
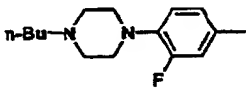


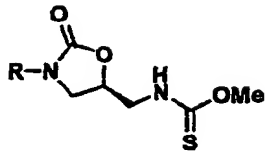
Example	R	Physical properties [recrystallization solvent]
2		colorless prisms [CH_3CN] mp,206～207℃ Elemental analysis for $C_{16}H_{20}FN_3O_4S_2$ Calcd. % : C,47.87;H,5.02;N,10.47 Found % : C,48.04;H,5.00;N,10.51 Specific rotation $[\alpha]_D^{20}$-25.0° (c=0.1,DMSO)
3		yellow liquid NMR(DMSO-d_6) δ ppm:3.19(4H,t,J=5.5Hz),3.51(4H,t,J=5.5Hz),3.80-3.90(3H,m),3.92(3H,s),4.10(1H,t,J=9Hz),4.80-4.90(1H,m),7.15-7.25(2H,m),7.43(1H,dd,J=13.5,2.5Hz),9.10(1H,br-s) MS(m/z):417(M^+) Specific rotation $[\alpha]_D^{20}$-23.9° (c=0.1,DMSO)
4		pale brown crystals[EtOH] mp,147～148.5℃ Elemental analysis for $C_{16}H_{20}FN_3O_3S$ Calcd. % : C,54.38;H,5.70;N,11.89 Found % : C,54.27;H,5.75;N,11.91 Specific rotation $[\alpha]_D^{20}$-26.9° (c=0.1,DMSO)
5		colorless crystals[EtOH] mp,131～133℃ Elemental analysis for $C_{16}H_{21}N_3O_3S_2$ Calcd. % : C,52.29;H,5.76;N,11.43 Found % : C,52.24;H,5.76;N,11.43 Specific rotation $[\alpha]_D^{20}$-24.1° (c=0.1,DMSO)
6		pale brown crystals[i-PrOH] mp,117～118℃ Elemental analysis for $C_{17}H_{22}FN_3O_3S$ Calcd. % : C,55.57;H,6.03;N,11.44 Found % : C,55.35;H,6.24;N,11.33 Specific rotation $[\alpha]_D^{20}$-29.1° (c=0.1,DMSO)

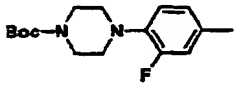
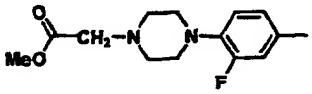
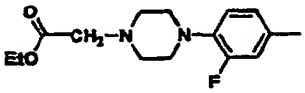
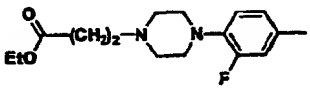
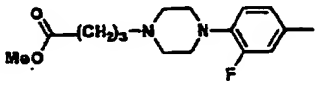
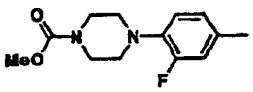


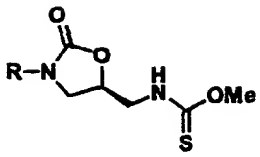
Example	R	Physical properties [recrystallization solvent]
7		pale brown needles [i-PrOH] mp,124.5~125.5℃ Elemental analysis for $C_{18}H_{24}FN_3O_3S$ Calcd. % : C,56.67;H,6.34;N,11.02 Found % : C,56.55;H,6.50;N,10.82 Specific rotation[α]$_D^{20}$-29.0° (c=0.1,DMSO)
8		pale brown needles [i-PrOH] mp,135~136℃ Elemental analysis for $C_{18}H_{24}FN_3O_3S$ Calcd. % : C,56.67;H,6.34;N,11.02 Found % : C,56.67;H,6.24;N,10.91 Specific rotation[α]$_D^{20}$-25.9° (c=0.1,DMSO)
9		colorless crystals [i-PrOH] mp,112~114℃ Elemental analysis for $C_{19}H_{26}FN_3O_3S$ Calcd. % : C,57.70;H,6.63;N,10.62 Found % : C,57.70;H,6.74;N,10.53 Specific rotation[α]$_D^{20}$-24.1° (c=0.1,DMSO)
10		colorless needles [i-PrOH] mp,112~113.5℃ Elemental analysis for $C_{18}H_{24}FN_3O_4S$ Calcd. % : C,54.39;H,6.09;N,10.57 Found % : C,54.19;H,6.21;N,10.47 Specific rotation[α]$_D^{20}$-24.1° (c=0.1,DMSO)
11		colorless crystals [i-PrOH] mp,138~140℃ Elemental analysis for $C_{19}H_{26}FN_3O_4S$ Calcd. % : C,55.46;H,6.37;N,10.21 Found % : C,55.65;H,6.58;N,10.15 Specific rotation[α]$_D^{20}$-32.9° (c=0.1,DMSO)
12		pale brown crystals [i-PrOH] mp,99~100.5℃ Elemental analysis for $C_{20}H_{28}FN_3O_5S$ Calcd. % : C,54.41;H,6.39;N,9.52 Found % : C,54.20;H,6.50;N,9.50 Specific rotation [α]$_D^{20}$-23.9° (c=0.1,DMSO)

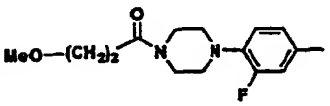
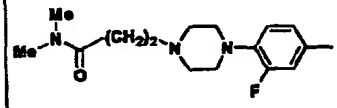
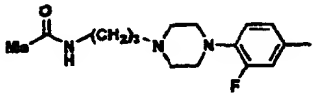
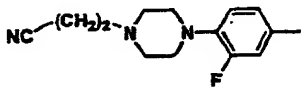
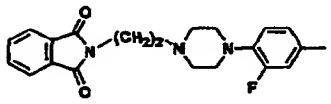


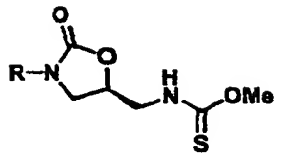
Example	R	Physical properties [recrystallization solvent]
13		colorless needles [i-PrOH] mp,110～112℃ Elemental analysis for $C_{16}H_{20}FN_3O_4S$ Calcd. % : C,52.02;H,5.46;N,11.37 Found % : C,52.02;H,5.42;N,11.27 Specific rotation [α]$_D^{20}$-27.0° (c=0.1,DMSO)
14		pale brown needles [i-PrOH] mp,79～80℃ Elemental analysis for $C_{18}H_{24}FN_3O_5S$ Calcd. % : C,52.29;H,5.85;N,10.16 Found % : C,52.20;H,5.66;N,10.19 Specific rotation [α]$_D^{20}$-25.0° (c=0.1,DMSO)
15		pale yellow crystals [i-PrOH-i-Pr$_2$O] mp,119.5～121.5℃ Elemental analysis for $C_{17}H_{23}FN_4O_3S$ Calcd. % : C,53.39;H,6.06;N,14.65 Found % : C,53.20;H,5.94;N,14.50 Specific rotation[α]$_D^{20}$-30.1° (c=0.1,DMSO)
16		pale brown crystals [i-PrOH] mp,122～123℃ Elemental analysis for $C_{18}H_{25}FN_4O_3S$ Calcd. % : C,54.53;H,6.36;N,14.13 Found % : C,54.29;H,6.10;N,14.02 Specific rotation [α]$_D^{20}$-19.1° (c=0.1,DMSO)
17		pale brown needles [i-PrOH] mp,128.5～129.5℃ Elemental analysis for $C_{19}H_{27}FN_4O_3S$ Calcd. % : C,55.59;H,6.63;N,13.65 Found % : C,55.36;H,6.57;N,13.57 Specific rotation [α]$_D^{20}$-25.0° (c=0.1,DMSO)
18		pale brown needles [i-PrOH] mp,118.5～120℃ Elemental analysis for $C_{20}H_{29}FN_4O_3S$ Calcd. % : C,56.58;H,6.89;N,13.20 Found % : C,56.50;H,7.03;N,13.14 Specific rotation [α]$_D^{20}$-22.0° (c=0.1,DMSO)

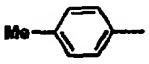
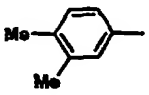
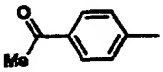
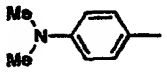
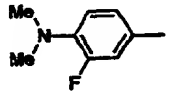


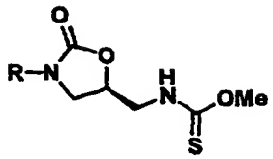
Example	R	Physical properties [recrystallization solvent]
19		colorless needles [i-PrOH] mp,153.5～155℃ Elemental analysis for $C_{21}H_{29}FN_4O_5S$ Calcd. % : C,53.83;H,6.24;N,11.96 Found % : C,53.83;H,6.17;N,11.85 Specific rotation $[\alpha]_D^{20}$-14.0° (c=0.1,DMSO)
20		colorless needles [i-PrOH] mp,147.5～149℃ Elemental analysis for $C_{19}H_{25}FN_4O_5S$ Calcd. % : C,51.81;H,5.72;N,12.72 Found % : C,51.76;H,5.59;N,12.53 Specific rotation $[\alpha]_D^{20}$-22.0° (c=0.1,DMSO)
21		colorless needles [i-PrOH] mp,126～127℃ Elemental analysis for $C_{20}H_{27}FN_4O_5S$ Calcd. % : C,52.85;H,5.99;N,12.33 Found % : C,52.82;H,5.75;N,12.22 Specific rotation $[\alpha]_D^{20}$-24.0° (c=0.1,DMSO)
22		pale yellow crystals [i-PrOH-i-Pr_2O] mp,98～99℃ Elemental analysis for $C_{21}H_{29}FN_4O_5S$ Calcd. % : C,53.83;H,6.24;N,11.96 Found % : C,53.75;H,6.26;N,11.93 Specific rotation $[\alpha]_D^{20}$-19.1° (c=0.1,DMSO)
23		colorless needles [i-PrOH] mp,97～98℃ Elemental analysis for $C_{21}H_{29}FN_4O_5S$ Calcd. % : C,53.83;H,6.24;N,11.96 Found % : C,53.77;H,6.34;N,11.89 Specific rotation $[\alpha]_D^{20}$-16.0° (c=0.1,DMSO)
24		colorless crystals [i-PrOH-i-Pr_2O] mp,114～116℃ Elemental analysis for $C_{18}H_{23}FN_4O_5S$ Calcd. % : C,50.69;H,5.44;N,13.14 Found % : C,50.85;H,5.53;N,12.88 Specific rotation $[\alpha]_D^{20}$-26.1° (c=0.1,DMSO)

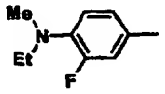
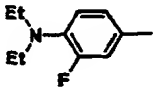
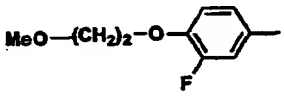
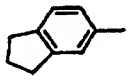
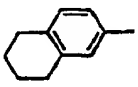


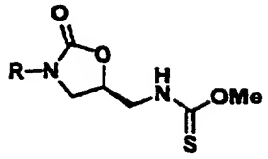
Example	R	Physical properties [recrystallization solvent]
25		pale reddish brown crystals [i-PrOH] mp,157～160℃ Elemental analysis for $C_{20}H_{27}FN_4O_5S$ Calcd. % : C,52.85;H,5.99;N,12.33 Found % : C,52.60;H,6.20;N,12.27 Specific rotation [α]$_D^{20}$-17.0° (c=0.1,DMSO)
26		pale brown crystals [i-PrOH] mp,173～174℃ Elemental analysis for $C_{21}H_{30}FN_5O_4S$ Calcd. % : C,53.95;H,6.47;N,14.98 Found % : C,53.72;H,6.78;N,14.71 Specific rotation [α]$_D^{20}$-21.0° (c=0.1,DMSO)
27		pale yellow liquid NMR(DMSO-d_6) δ ppm:1.57(2H,quin,J=7.5Hz), 1.79(3H,s),2.34(2H,t,J=7.5Hz),2.50(4H,t,J=4.5Hz),2.98(4H,t,J=4.5Hz),3.00-3.10(2H,m),3.45-3.55(2H,m),3.75-3.85(1H,m),3.89(3H,s),4.11(1H,t,J=9Hz),4.85-4.95(1H,m),7.03(1H,t,J=9Hz),7.17(1H,dd,J=9,2.5Hz),7.46(1H,dd,J=14.5,2.5Hz),7.68(1H,br-s),8.39(1H,br-s) IR ν (liq.) cm^{-1}:1748,3304 Specific rotation[α]$_D^{20}$-50.6° (c=0.1,DMSO)
28		colorless crystals [i-PrOH] mp,115～117℃ Elemental analysis for $C_{19}H_{24}FN_5O_3S$ Calcd. % : C,54.14;H,5.74;N,16.62 Found % : C,54.08;H,5.93;N,16.51 Specific rotation [α]$_D^{20}$-24.0° (c=0.1,DMSO)
29		pale brown crystals [DMF-H_2O] mp,193.5～195℃ Elemental analysis for $C_{26}H_{28}FN_5O_5S$ Calcd. % : C,57.66;H,5.21;N,12.93 Found % : C,57.64;H,5.20;N,12.77 Specific rotation [α]$_D^{20}$-19.1° (c=0.1,DMSO)

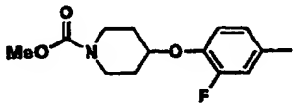
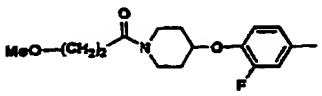
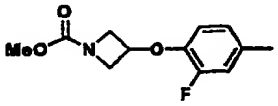
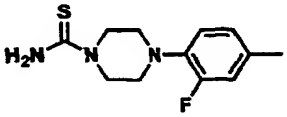


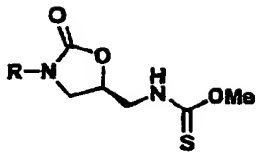
Example	R	Physical properties [recrystallization solvent]
30		colorless crystals[i-Pr_2O] mp,102.5～103.5℃ Elemental analysis for $C_{13}H_{16}N_2O_3S$ Calcd. % : C,55.70;H,5.75;N,9.99 Found % : C,55.86;H,6.02;N,9.89 Specific rotation[α]$_D^{20}$-33.9° (c=0.1,DMSO)
31		colorless needles[i-PrOH] mp,108～110℃ Elemental analysis for $C_{14}H_{18}N_2O_3S$ Calcd. % : C,57.12;H,6.16;N,9.52 Found % : C,57.29;H,6.38;N,9.51 Specific rotation[α]$_D^{20}$-32.0° (c=0.1,DMSO)
32		pale yellow needles[i-PrOH] mp,146.5～148.5℃ Elemental analysis for $C_{14}H_{16}N_2O_4S$ Calcd. % : C,54.53;H,5.23;N,9.08 Found % : C,54.51;H,5.11;N,9.05 Specific rotation[α]$_D^{20}$-45.0° (c=0.1,DMSO)
33		pale brown crystals[i-PrOH] mp,149～150℃ Elemental analysis for $C_{14}H_{19}N_3O_3S$ Calcd. % : C,54.35;H,6.19;N,13.58 Found % : C,54.54;H,6.14;N,13.45 Specific rotation [α]$_D^{20}$-24.0° (c=0.1,DMSO)
34		pale yellow liquid NMR(DMSO-d_6) δ ppm:2.77(6H,s),3.75-3.85(3H,m),3.92(3H,s),4.06(1H,t,J=9Hz),4.80-4.90(1H,m),6.95(1H,t,J=9Hz),7.13(1H,dd,J=9,2.5Hz),7.40(1H,dd,J=15.5,2.5Hz),9.10(1H,br-s) IR ν (liq.) cm^{-1}:1754,3268 MS(m/z):327(M^+) Specific rotation[α]$_D^{20}$-38.1° (c=0.1,DMSO)

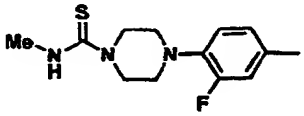
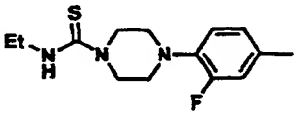
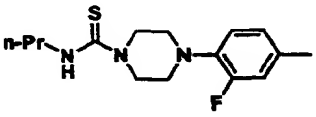
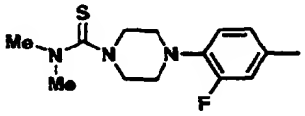
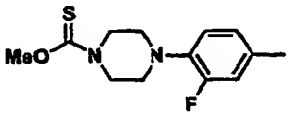


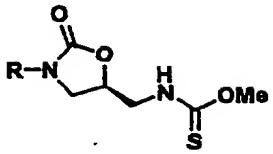
Example	R	Physical properties [recrystallization solvent]
35		pale brown needles[i-PrOH] mp,91～92℃ Elemental analysis for $C_{15}H_{20}FN_3O_3S$ Calcd. % : C,52.77;H,5.90;N,12.31 Found % : C,52.83;H,6.16;N,12.26 Specific rotation $[\alpha]_D^{20}$-25.1° (c=0.1,DMSO)
36		pale brown liquid NMR(DMSO-d_6) δ ppm:1.01(6H,t,J=7Hz),3.13(4H,q,J=7Hz),3.70-3.85(3H,m),3.92(3H,s),4.09(1H,t,J=9Hz),4.80-4.90(1H,m),7.01(1H,t,J=9Hz),7.10-7.20(1H,m),7.36(1H,dd,J=14.5,2.5Hz),9.10(1H,br-s) IR ν (liq.) cm^{-1}: 1378,1460 MS(m/z):355(M^+) Specific rotation $[\alpha]_D^{20}$-35.8° (c=0.1,DMSO)
37		colorless needles[EtOH] mp,101～102℃ Elemental analysis for $C_{15}H_{19}FN_2O_5S$ Calcd. % : C,50.27;H,5.34;N,7.82 Found % : C,50.22;H,5.36;N,7.81 Specific rotation $[\alpha]_D^{20}$-33.0° (c=0.1,DMSO)
38		pale brown prisms[i-PrOH] mp,134～135℃ Elemental analysis for $C_{15}H_{18}N_2O_3S$ Calcd. % : C,58.80;H,5.92;N,9.14 Found % : C,58.94;H,6.04;N,9.16 Specific rotation $[\alpha]_D^{20}$-31.0° (c=0.1,DMSO)
39		pale brown prisms[i-PrOH] mp,145.5～147℃ Elemental analysis for $C_{16}H_{20}N_2O_3S$ Calcd. % : C,59.98;H,6.29;N,8.74 Found % : C,60.10;H,6.40;N,8.70 Specific rotation $[\alpha]_D^{20}$-35.1° (c=0.1,DMSO)

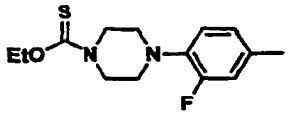
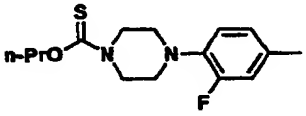
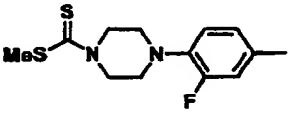
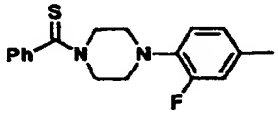


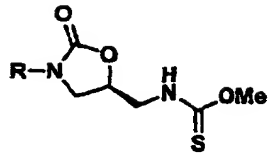
Example	R	Physical properties [recrystallization solvent]
40		yellow liquid NMR(DMSO-d_6) δ ppm:1.55-1.65(2H,m),1.80-1.95(2H,m),3.20-3.30(2H,m),3.61(3H,s),3.60-3.70(2H,m),3.70-3.85(3H,m),3.92(3H,s),4.10(1H,t,J=8.5Hz),4.40-4.50(1H,m),4.80-4.90(1H,m),7.15-7.25(2H,m),7.40-7.50(1H,m),9.10(1H,br-s) IR ν (liq.) cm^{-1}:1696,1756 Specific rotation[α]$_D^{20}$-20.7° (c=0.1,DMSO)
41		colorless amorphous solid NMR(DMSO-d_6) δ ppm:1.55-1.65(2H,m),1.85-1.95(2H,m),2.56(2H,t,J=6.5Hz),3.24(3H,s),3.25-3.35(2H,m),3.58(2H,t,J=6.5Hz),3.70-3.85(3H,m),3.92(3H,s),4.10(1H,t,J=9Hz),4.45-4.55(1H,m),4.80-4.90(1H,m),7.15-7.25(2H,m),7.47(1H,d,J=13Hz),9.11(1H,br-s) IR ν (liq.) cm^{-1}:1756 Specific rotation[α]$_D^{20}$-17.2° (c=0.1,DMSO)
42		pale yellow prisms[EtOH] mp,177～178.5℃ Elemental analysis for $C_{17}H_{20}FN_3O_6S$ Calcd. % : C,49.39;H,4.88;N,10.16 Found % : C,49.23;H,4.79;N,10.07 Specific rotation [α]$_D^{20}$-24.0° (c=0.1,DMSO)
43		colorless crystals NMR(DMSO-d_6) δ ppm:3.03(4H,t,J=5Hz),3.75-3.85(3H,m),3.85-3.90(4H,m),3.91(3H,s),4.11(1H,t,J=9Hz),4.80-4.90(1H,m),7.06(1H,t,J=9Hz),7.13(2H,br-s),7.17(1H,dd,J=9,2.5Hz),7.43(1H,dd,J=15.5,2.5Hz),9.11(1H,br-s) IR ν (KBr) cm^{-1}:3272 Specific rotation[α]$_D^{20}$-60.1° (c=0.1,DMSO)

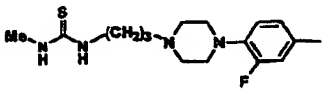
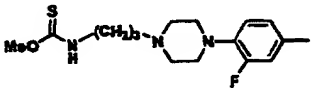
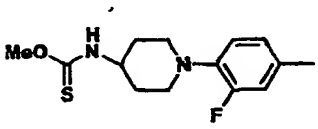


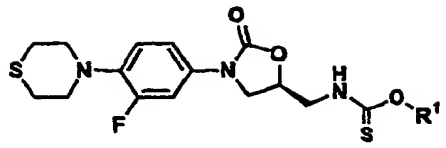
Example	R	Physical properties [recrystallization solvent]
44		pale brown needles[EtOH] mp,168~169℃ Elemental analysis for $C_{18}H_{24}FN_5O_3S_2$ Calcd. % : C,48.96;H,5.48;N,15.86 Found % : C,48.82;H,5.26;N,15.76 Specific rotation[α]$_D^{20}$-24.0° (c=0.1,DMSO)
45		pale brown needles[CH_3CN] mp,157~158.5℃ Elemental analysis for $C_{19}H_{26}FN_5O_3S_2$ Calcd. % : C,50.09;H,5.75;N,15.37 Found % : C,50.10;H,5.69;N,15.26 Specific rotation[α]$_D^{20}$-28.0° (c=0.1,DMSO)
46		colorless crystals[MeOH] mp,162.5~164.5℃ Elemental analysis for $C_{20}H_{28}FN_5O_3S_2$ Calcd. % : C,51.15;H,6.01;N,14.91 Found % : C,51.07;H,5.87;N,14.90 Specific rotation[α]$_D^{20}$-21.1° (c=0.1,DMSO)
47		pale brown crystals NMR(DMSO-d_6) δ ppm:3.09(4H,t,J=5Hz),3.11(6H,s),3.51(4H,t,J=5Hz),3.75-3.85(3H,m),3.92(3H,s),4.10(1H,t,J=9Hz),4.80-4.90(1H,m),7.07(1H,t,J=9Hz),7.18(1H,dd,J=9,2Hz),7.42(1H,dd,J=14.5,2Hz),9.11(1H,br-s) IR ν (KBr) cm^{-1}:1748,3392 Specific rotation[α]$_D^{20}$-21.9° (c=0.1,DMSO)
48		colorless needles[i-PrOH] mp,181~182.5℃ Elemental analysis for $C_{18}H_{23}FN_4O_4S_2$ Calcd. % : C,48.85;H,5.24;N,12.66 Found % : C,49.04;H,5.13;N,12.71 Specific rotation[α]$_D^{20}$-32.1° (c=0.1,DMSO)



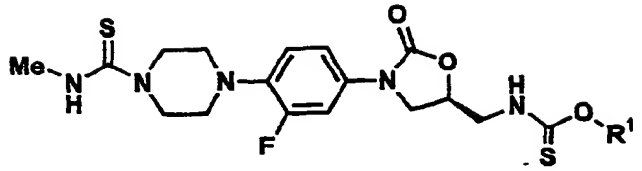
Example	R	Physical properties [recrystallization solvent]
49		colorless crystals [EtOH] mp,126.5～127℃ Elemental analysis for $C_{19}H_{25}FN_4O_4S_2$ Calcd. % : C,49.98;H,5.52;N,12.27 Found % : C,49.87;H,5.69;N,12.27 Specific rotation $[\alpha]_D^{20}$-25.9° (c=0.1,DMSO)
50		colorless crystals [MeOH] mp,148～149℃ Elemental analysis for $C_{20}H_{27}FN_4O_4S_2$ Calcd. % : C,51.05;H,5.78;N,11.91 Found % : C,51.16;H,5.81;N,11.70 Specific rotation $[\alpha]_D^{20}$-24.0° (c=0.1,DMSO)
51		colorless crystals [i-PrOH] mp,160～162℃ Elemental analysis for $C_{18}H_{23}FN_4O_3S_3$ Calcd. % : C,47.14;H,5.06;N,12.22 Found % : C,47.40;H,5.04;N,12.13 Specific rotation $[\alpha]_D^{20}$-22.9° (c=0.1,DMSO)
52		yellow needles [AcOEt] mp,148～149℃ Elemental analysis for $C_{23}H_{25}FN_4O_3S_2$ Calcd. % : C,56.54;H,5.16;N,11.47 Found % : C,56.39;H,5.10;N,11.32 Specific rotation $[\alpha]_D^{20}$-25.0° (c=0.1,DMSO)



Example	R	Physical properties [recrystallization solvent]
53		colorless amorphous solid NMR(DMSO-d6) δ ppm:1.69(2H,quin,J=6.5Hz),2.39(2H,t,J=6.5Hz),2.54(4H,t,J=5Hz),2.85(3H,d,J=4.5Hz),3.03(4H,t,J=5Hz),3.40-3.50(2H,m),3.70-3.85(3H,m),3.92(3H,s),4.08(1H,t,J=9Hz),4.80-4.90(1H,m),7.03(1H,t,J=9Hz),7.12(1H,br-s),7.15(1H,dd,J=9,2.5Hz),7.16(1H,br-s),7.39(1H,dd,J=15,2.5Hz),9.10(1H,br-s) IR ν (KBr) cm-1:1746,3252 Specific rotation [α]D20-20.9° (c=0.1,DMSO)
54		pale brown liquid NMR(DMSO-d6) δ ppm:1.60-1.80(2H,m),2.39(2H,t,J=6.5Hz),2.53(4H,t,J=5Hz),3.02(4H,t,J=5Hz),3.40-3.50(2H,m),3.70-3.85(3H,m),3.87(3H,s),3.92(3H,s),4.08(1H,t,J=9Hz),4.80-4.90(1H,m),7.02(1H,t,J=9Hz),7.15(1H,dd,J=9,2.5Hz),7.39(1H,dd,J=15.5,2.5Hz),8.77(1H,br-s),9.10(1H,br-s) IR ν (liq.) cm-1:1740,3268 Specific rotation [α]D20-18.1° (c=0.1,DMSO)
55		pale brown crystals NMR(DMSO-d6) δ ppm:1.60-1.75(2H,m),1.90-2.05(1H,m),2.40-2.55(2H,m),2.70-2.85(2H,m),3.25-3.35(2H,m),3.65-3.85(3H,m),3.89(3H,s),3.92(3H,s),4.08(1H,t,J=9Hz),4.80-4.90(1H,m),7.05(1H,t,J=9Hz),7.14(1H,dd,J=9,2.5Hz),7.39(1H,dd,J=14.5,2.5Hz),8.80(1H,br-s),9.11(1H,br-s) IR ν (KBr) cm-1:1740,3272 Specific rotation [α]D20-25.0° (c=0.1,DMSO)



Example	R^1	Physical properties [recrystallization-solvent]
56	Et	colorless crystals [i-PrOH] mp,103.5～104.5℃ Elemental analysis for $C_{17}H_{22}FN_3O_3S_2$ Calcd. % : C,51.11;H,5.55;N,10.52 Found % : C,51.20;H,5.67;N,10.38 Specific rotation [α]$_D^{20}$-23.1° (c=0.1,DMSO)
57	n-Pr	pale yellow crystals [i-PrOH] mp,124～125℃ Elemental analysis for $C_{18}H_{24}FN_3O_3S_2$ Calcd. % : C,52.28;H,5.85;N,10.16 Found % : C,52.22;H,5.86;N,10.12 Specific rotation [α]$_D^{20}$-30.9° (c=0.1,DMSO)
58	i-Pr	colorless crystals [i-PrOH-i-Pr$_2$O] mp,164～166℃ Elemental analysis for $C_{18}H_{24}FN_3O_3S_2$ Calcd. % : C,52.28;H,5.85;N,10.16 Found % : C,52.06;H,5.56;N,10.01 Specific rotation [α]$_D^{20}$-32.1° (c=0.1,DMSO)
59	cyc-Hex	pale yellow crystals [MeOH] mp,150～152℃ Elemental analysis for $C_{21}H_{28}FN_3O_3S_2$ Calcd. % : C,55.61;H,6.22;N,9.26 Found % : C,55.49;H,5.97;N,9.07 Specific rotation [α]$_D^{20}$-26.9° (c=0.1,DMSO)



Example	R^1	Physical properties [recrystallization solvent]
60	Et	pale yellow prisms [EtOH] mp,152~153°C Elemental analysis for $C_{19}H_{26}FN_5O_3S_2$ Calcd. % : C,50.09;H,5.75;N,15.37 Found % : C,50.14;H,5.82;N,15.13 Specific rotation $[\alpha]_D^{20}$-30.0° (c=0.1,DMSO)

Example 61

[0140] O-Methyl (S)-N-[3-[3-fluoro-4-[4-(3-mesylaminopropyl)piperazin-1-yl]-phenyl]-2-oxooxazolidin-5-yl]methylthiocarbamate

1) To a solution of 0.40 g of (S)-5-aminomethyl-3-[3-fluoro-4-[4-(3-mesylaminopropyl)piperazin-1-yl]phenyl]-2-oxooxazolidine and 0.13 ml of triethylamine in 4 ml of dried tetrahydrofuran, 0.12 ml of carbon disulfide was added under ice-cooling and with stirring, and the mixture was stirred at the same temperature for 5 hours. The mixture was added with 0.09 ml of ethyl chlorocarbonate under ice-cooling and with stirring, and further stirred at the same temperature for 2 hours. The reaction solution was added with water, and extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure to obtain 0.39 g of a pale brown amorphous solid.
2) To 3.5 ml of dried methanol, 0.06 g of 60 % sodium hydride was added under stirring at room temperature, and the mixture was stirred at room temperature for 30 minutes. Then, the mixture was added with 0.35 g of the amorphous solid obtained in 1), and stirred at room temperature for 1 hour. The reaction mixture was neutralized with ice water and 10 % hydrochloric acid, and extracted with ethyl acetate. The extract was washed with saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (alumina, ethyl acetate) to obtain 0.14 g of pale brown crystals. Recrystallization from isopropanol gave colorless needles having the melting point of from 120 to 121.5°C.

Elemental analysis for $C_{20}H_{30}FN_5O_5S_2$						
Calculated %	C,	47.70;	H,	6.00;	N,	13.91
Found %	C,	47.76;	H,	5.88;	N,	13.70

Specific rotation $[\alpha]_D^{20}$ -19.0° (c = 0.1, DMSO)

Example 62

[0141] O-Methyl (S)-N-[3-[3-fluoro-4-(piperazin-1-yl)phenyl]-2-oxooxazolidin-5-yl]-methylthiocarbamate

[0142] To 4 ml of 10 % hydrogen chloride ethyl acetate solution, 0.20 g of O-methyl (S)-N-[3-[4-(4-tert-butoxycarbonylpiperazin-1-yl)-3-fluorophenyl]-2-oxooxazolidin-5-yl]methylthiocarbamate was added under ice-cooling and with stirring, and the mixture was stirred at room temperature for 6 hours. After the reaction, the solvent was evaporated under reduced pressure, and the residue was added with aqueous sodium hydrogencarbonate, and extracted with 1,2-dichloroethane. The extract was washed successively with water and saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure to obtain 0.10 g of a colorless amorphous solid.
NMR spectrum (DMSO-d_6) δ ppm:
3.00(8H,s),3.21(1H,br-s),3.75-3.85(3H,m),3.89(3H,s),4.11(1H,t,J=9Hz), 4.85-4.90(1H,m),7.07(1H,t,J=9.5Hz),7.15-

7.19(1H,m),7.45(1H,dd,J=15,3Hz), 9.39(1H,br-s)
IR spectrum ν (KBr) cm^{-1}: 1750,3228
Specific rotation $[\alpha]_D^{20}$ -30.1° (c = 0.1, DMSO)

Example 63

[0143] O-Methyl (S)-N-[3-[3-fluoro-4-[4-(3-oxobutyl)piperazin-1-yl]phenyl]-2-oxo-oxazolidin-5-yl]methylthiocarbamate

[0144] To a solution of O-methyl (S)-N-[3-[3-fluoro-4-(piperazin-1-yl)phenyl]-2-oxo-oxazolidin-5-yl]methylthiocarbamate in 1 ml of methanol, 0.01 ml of methyl vinyl ketone was added under stirring at room temperature, and the mixture was stirred at the same temperature for 30 minutes. After the reaction, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (alumina, ethyl acetate) to obtain 0.06 g of colorless crystals.
NMR spectrum ($CDCl_3$) δ ppm:
2.19(3H,s),2.63(4H,t,J=5Hz),2.66(2H,t,J=6.5Hz),2.74(2H,t,J=6.5Hz),3.07(4H,t,J=5Hz), 3.82(1H,dd,J=9,6.5Hz),4.00(3H,s),3.90-4.15(3H,m),4.85-4.95(1H,m),6.69(1H,t,J=6Hz), 6.92(1H,t,J=9Hz),7.07(1H,dd,J=9,2.5Hz)17.41(1H,dd,J=14,2.5Hz)
IR spectrum ν (KBr) cm^{-1}: 1714,1746,3284
Specific rotation $[\alpha]_D^{20}$ -20.8° (c = 0.1, DMSO)

Example 64

[0145] O-Methyl (S)-N-[3-[4-(4-carbamoylpiperazin-1-yl)-3-fluorophenyl]-2-oxo-oxazolidin-5-yl]methylthiocarbamate

[0146] To a solution of 0.50 g of O-methyl (S)-N-[3-[3-fluoro-4-(piperazin-1-yl)-phenyl]-2-oxooxazolidin-5-yl]methylthiocarbamate in 5.0 ml of acetic acid, a solution of 0.21 g of sodium cyanate in 5.0 ml of water was added under stirring at room temperature, and the mixture was stirred at the same temperature for 2 hours. The reaction solution was neutralized with 40% aqueous sodium hydroxide, and then extracted with ethyl acetate. The extract was washed successively with water and saturated brine, and dried over sodium sulfate, and then the solvent was evaporated under reduced pressure. The residue was washed with ethyl acetate to obtain 0.15 g of colorless crystals.
NMR spectrum (DMSO-d_6) δ ppm:
2.90-3.00(4H,m),3.40-3.50(5H,m),3.70-3.85(2H,m),3.92(3H,s),4.09(1H,t,J=9Hz), 4.70-4.90(1H,m),5.64(2H,br-s), 7.05(1H,t,J=9Hz),7.10-7.20(1H,m), 7.41(1H,dd,J=14.5,2.5Hz),9.10(1H,br-s)
IR spectrum ν (KBr) cm^{-1}: 1740
Specific rotation $[\alpha]_D^{20}$ -32.0° (c = 0.1, DMSO)

Example 65

[0147] O-Methyl (S)-N-[3-[3-fluoro-4-(4-thioacetylpiperazin-1-yl)phenyl]-2-oxooxazolidin-5-yl]methylthiocarbamate

[0148] To a solution of 0.50 g of O-methyl (S)-N-[3-[3-fluoro-4-(piperazin-1-yl)-phenyl]-2-oxooxazolidin-5-yl]methylthiocarbamate in 5.0 ml of tetrahydrofuran, 0.17 ml of ethyl dithioacetate was added under stirring at room temperature, and the mixture was stirred at the same temperature for 18 hours. After the reaction, the solvent was evaporated under reduced pressure, and the residue was washed with ethyl acetate to obtain 0.27 g of colorless crystals. Recrystallization from acetonitrile gave colorless crystals having the melting point of from 176 to 178°C.

Elemental analysis for $C_{18}H_{23}FN_4O_3S_2$						
Calculated %	C,	50.69;	H,	5.44;	N,	13.14
Found %	C,	50.71;	H,	5.34;	N,	13.26

Specific rotation $[\alpha]_D^{20}$ -33.0° (c = 0.1, DMSO)

[0149] To evaluate excellent effectiveness of the thiocarbamic acid derivatives of the present invention, antibacterial tests against type strains, clinical isolates, and atypical acid-fast bacteria were performed.

[Antibacterial spectra against type strains, clinical isolates, and atypical acid-fast bacteria]

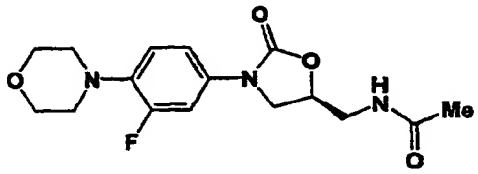
[0150] Antibacterial activities (minimum inhibitory concentration: MIC) were determined according to the standard method of the Japan Society of Chemotherapy [Chemotherapy, Vol. 29, p.76 (1981)] by using type strains and strains

isolated from patients with infectious disease (including clinical isolates and atypical acid-fast bacteria), and applying 10^6/ml of colony forming bacteria. Linezolid was used as the reference compound [a compound described in Journal of Medicinal Chemistry, Vol. 39, p.673 (1996), hereinafter referred to as "reference compound"].

[0151] The compounds of the present invention had excellent antibacterial activities compared to the referenc compound against type strains, clinical isolates, and atypical acid-fast bacteria.

[0152] Names of the bacteria in the table are as follows:

Type strain	*Staphylococcus aureus (S. aureus) Bacillus subtilis (B. subtilis)*
Clinical isolates	Methicillin-resistant *Staphylococcus aureus* (MRSA) *Staphylococcus epidermidis (S. epidermidis) Enterococcus faecalis (E. faecalis) Enterococcus faecium (E. faecium)*
Atypical acid-fast	bacteria *Mycobacterium avium (M. avium) Mycobacterium intracellulare (M. intracellulare)*



Reference compound(Linezolid)

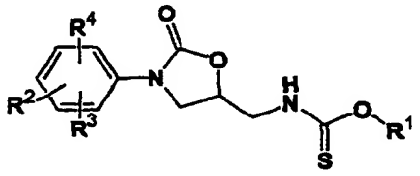
Antibacterial spectrum against type strains (MIC μg/ml)					
Compound / Names of bacteria	Example 1	Example 2	Example 3	Example 4	Reference compound
S.aureus Smith HPC023	1.56	0.78	0.78	0.39	3.13
S.aureus MS353 HPC017	0.78	0.78	0.78	0.39	3.13
B.subtilis ATCC 6633 HPR022	0.39	0.39	0.39	0.39	0.78
Antibacterial spectrum against clinical isolates (MIC μg/ml)					
Compound / Names of bacteria	Example 1	Example 2	Example 3	Example 4	Reference compound
MRSA HPC 432	0.78	0.78	0.78	0.39	3.13
MRSA HPC 1336	0.78	0.78	0.78	0.39	3.13
S.epidermidis HPC 1728	0.78	0.78	0.39	0.39	3.13
E.faecalis HPC 1321	0.78	0.39	0.39	0.39	1.56
E.faecium HPC 1322	0.78	0.39	0.39	0.39	1.56
Antibacterial spectrum against atypical acid-fast bacteria (MIC μg/ml)					
Compound / Names of bacteria	Example 1	Example 2	Example 3	Example 4	Reference compound
M.avium 20092	0.39	3.13	3.13	1.56	25
M.avium 20096	0.39	3.13	3.13	1.56	50
M.intracellulare 20067	0.39	6.25	3.13	1.56	12.5
M.intracellulare 20073	0.39	6.25	3.13	0.78	6.25

Industrial Applicability

[0153] The novel thiocarbamic acid derivatives or salts thereof according to the present invention have excellent antibacterial activity against clinical isolates and atypical acid-fast bacteria including multiple drug-resistant bacteria as w ll as type strains, and are extremely useful as antibacterial agents.

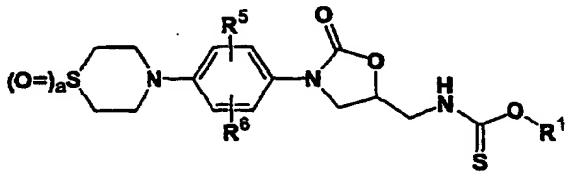
Claims

1. A thiocarbamic acid derivative represented by the following general formula or a salt thereof:



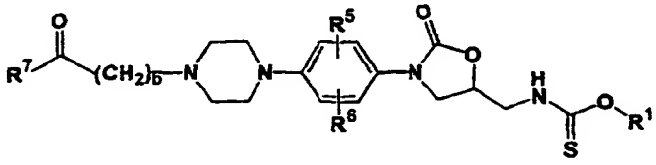
wherein R^1 represents an alkyl group which may be substituted, or a cycloalkyl group which may be substituted; and R^2, R^3, and R^4 independently represent hydrogen atom, a halogen atom, an alkyl group which may be substituted, an alkoxyl group which may be substituted, an amino group which may be substituted, an alkanoyl group which may be substituted, a cycloalkyloxy group which has a heteroatom as a ring constituting atom and which may be substituted, or a saturated heterocyclic group which may be substituted; or any two of R^2, R^3, and R^4 may bind to each other to form, together with the benzene ring, a condensed hydrocarbon ring which may be substituted.

2. A thiocarbamic acid derivative represented by the following general formula or a salt thereof:



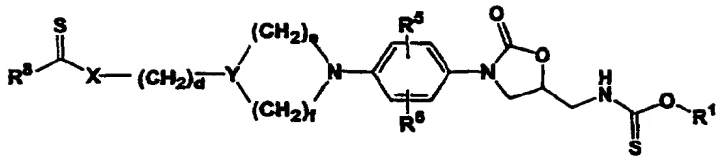
wherein R^1 represents an alkyl group which may be substituted, or a cycloalkyl group which may be substituted; R^5 and R^6 independently represent hydrogen atom, or a halogen atom; and symbol "a" represents an integer of from 0 to 2.

3. A thiocarbamic acid derivative represented by the following general formula or a salt thereof:



wherein R^1 represents an alkyl group which may be substituted, or a cycloalkyl group which may be substituted; R^5 and R^6 independently represent hydrogen atom, or a halogen atom; R^7 represents an alkyl group which may be substituted, an amino group which may be substituted, or an alkoxyl group which may be substituted; and symbol "b" represents an integer of from 1 to 4.

4. A thiocarbamic acid derivative represented by the following general formula or a salt thereof:



wherein R^1 represents an alkyl group which may be substituted, or a cycloalkyl group which may be substituted; R^5 and R^6 independently represent hydrogen atom, or a halogen atom; R^8 represents an alkyl group which may be substituted, a cycloalkyl group which may be substituted, an alkenyl group which may be substituted, an alkynyl group which may be substituted, an alkoxyl group which may be substituted, an alkylthio group which may be substituted, an amino group which may be substituted, a saturated heterocyclic group which may be substituted, an aryl group which may be substituted, or an aralkyl group which may be substituted; Y represents CH or nitrogen atom; X represents NH or single bond; symbol "d" represents an integer of from 0 to 3; and symbols "e" and "f" independently represent an integer of from 1 to 3.

5. A medicament which comprises the compound or a salt thereof according to any one of claims 1 to 4 as an active ingredient.

6. The medicament according to claim 5 which is an antibacterial agent.

7. A use of the compound or a salt thereof according to any one of claims 1 to 4 for the manufacture of the medicament according to claim 5 or 6.

8. A method for preventive and/or therapeutic treatment of an infectious disease, which comprises the step of administering a preventively and/or therapeutically effective amount of the compound or a salt thereof according to any one of claims 1 to 4 to a mammal including a human.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP99/06260

A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl[7] C07D263/22, C07D413/12, C07D417/10, A61K31/421, A61K31/435, A61K31/445, A61K31/496, A61K31/541, A61K31/55, A61K31/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int.Cl[7] C07D263/22, C07D413/12, C07D417/10, A61K31/421, A61K31/435, A61K31/445, A61K31/496, A61K31/541, A61K31/55, A61K31/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAPLUS (STN)
REGISTRY (STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PX	WO, 98/54161, A1 (Pharmacia & Upjohn Company), 03 December, 1998 (03.12.98) & AU, 9874883, A1	1-7
A	EP, 789025, A1 (Bayer A.-G.), 13 August, 1997 (13.08.97) & DE, 19604223, A1 & US, 5792765, A & JP, 9-316073, A	1-7

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
04 February, 2000 (04.02.00)	22 February, 2000 (22.02.00)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP99/06260

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 8
because they relate to subject matter not required to be searched by this Authority, namely:

The subject matter of claim 8 relates to a method for treatment of the human or animal body by therapy, which does not require an international search report by this International Search Authority in accordance with PCT Article 17(2) (a)(i) and Rule 39.1(iv).

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1992)